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SOUTH KOREA's EXPERIENCE OF REIMBURSING HIGH-COST MEDICINES

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Key messages

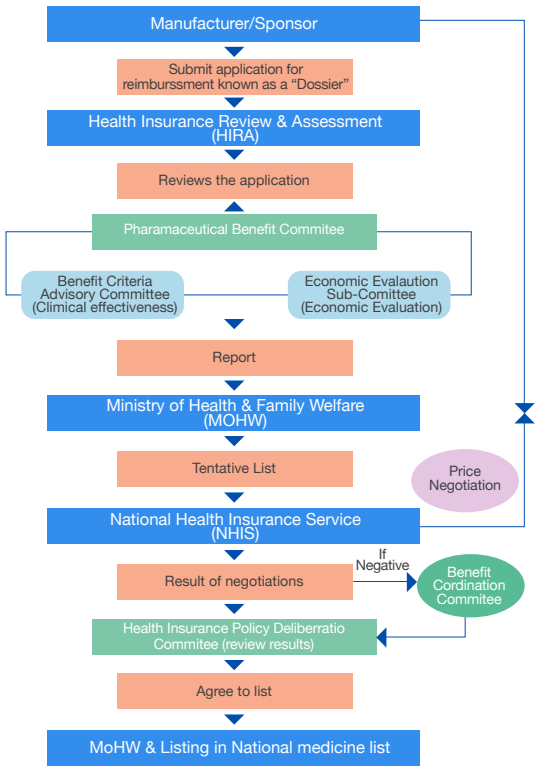
- Cost-effectiveness and availability of alternative treatment options play a crucial role in the listing of new medicines in South Korea. However, high-cost medicines with **no alternative treatment options**, particularly those for treating **cancer and rare diseases,** were not reimbursed under the traditional route.
- To address this issue, the government of South Korea introduced several reforms to facilitate the reimbursement of high-cost medicines, including the **listing of essential medicines, RSA, price negotiation waivers, and PE exemptions.**
- These mechanisms have enabled increased access to high-cost medicines and reduced the time between market approval and reimbursement decisions. However, there is potential for improvement and issues around confidentiality of agreements and transparency of price raised by stakeholders that need to be addressed.

South Korea's approach to expanding access to high-cost medicines

System for reimbursing new medicines

South Korea implemented the National Health Insurance (NHI) programme in 1963 and gradually expanded its scope to achieve Universal Health Coverage (UHC) (1). It is mandatory for all citizens to participate in the national insurance system and a co-pay of 5-60% of the medical cost is often applicable to patients. In order to manage the health budget more efficiently, the NHI introduced the Positive Listing system (PLS) in 2007 to rationalise the distribution of medicines and therapeutics and curtail the medicine expenditure (2). After the implementation of PLS, only clinically and economically viable medicines that were cost effective were reimbursed, and prices were set through price-negotiations between the National Health Insurance Service (NHIS), the insurer, and pharmaceutical companies, in collaboration with the Health Insurance Review and Assessment (HIRA) and the Ministry of Health and Family Welfare (MoHFW)[3]. Figure 1, adapted from Young Bae[4], explains the governance structure of different agencies responsible for pricing and listing of new medicines under the NHI.

Figure 1. Governance structure for listing and pricing of new medicines in South Korea



HIRA, Health Insurance Review and Assessment Service; MOHW, Ministry of Health and Welfare; NHIs, National Health Insurance service

[Adapted from] Bae E-Y. Role of Health Technology Assessment in Drug Policies: Korea. Value in Health Regional Issues. 2019;18:24-9]

Challenges and reform

Although South Korea was the first country in the Asian region to adopt economic evaluation to inform the reimbursement of new medicines, it has been observed that high-priced medicines with uncertain cost-effectiveness are often unavailable to patients due to their cost-ineffectiveness. Consequently, the reimbursement acceptance rate for reimbursement for oncology and rare disease medicines was as low as 39% and 42% respectively [5, 6]. For example, XOLAIR (omalizumab), an orphan medicine for treating severe allergic asthma, remained non-reimbursable due to uncertainty in its cost-effectiveness evidence, with the longest waiting period of 11 years for reimbursement [7].

However, high-cost medicines became available after the introduction of yet another policy reform in 2013 known as the "Introduction of the Benefit Enhancement Plan" (IBEP) which covers four major conditions namely, cancers, cardiovascular diseases, cerebrovascular diseases, and rare diseases [8]. This scheme applies a higher incremental cost-effectiveness ratio (ICER) threshold for medicines with no alternative forms of treatment for these four conditions.

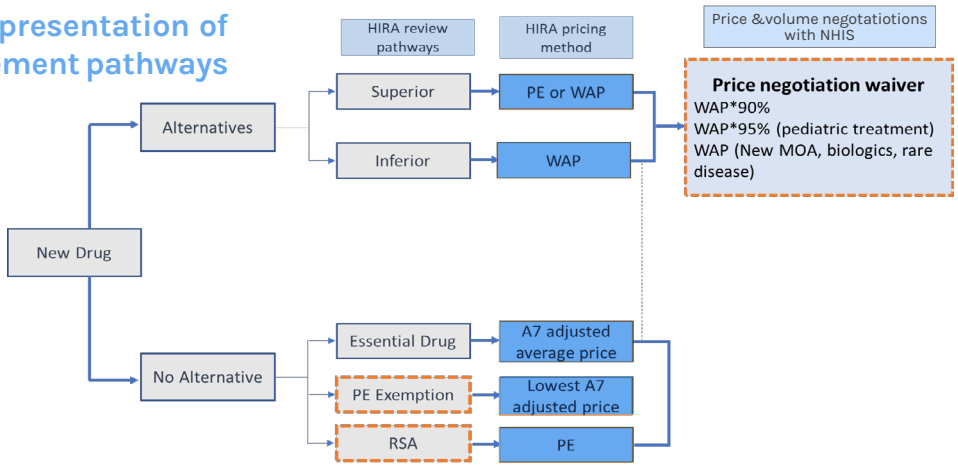
The government of South Korea introduced the IBEP reform in consultation with HIRA, which establishes guidelines for economic evaluation[9]. In addition to implementing a higher ICER threshold for medicines that meet the pre-defined criteria (Table 1), high-cost medicines may be reimbursed through other **alternative pricing and reimbursement (P&R) pathways** including; a) listing as essential medicines; b) risk-sharing agreements (RSA) for high priced medicines with no alternatives (primarily cancer medicines); c) pharmacoeconomic evaluation (PE) exemption for medicines with limited clinical evidence, indicated for life threatening conditions, with no alternative treatments and d) price negotiation waivers to expediate the launching of new medicines [3], as detailed below.

Pricing and reimbursement pathways for the high-cost medicines

The P&R process for any new medicine is typically determined by comparing it with available alternative treatments. Alternatives are defined as medicines currently used for an equivalent therapeutic indication[3, 10]. **For a medicine with therapeutic alternatives,** there are typically two pathways for reimbursement based on comparative effectiveness evidence: a) PE evaluation; and b) negotiation with the NHIS based on weighted average price (WAP) of alternative medicines. The medicine with proven clinical superiority is first evaluated for its cost effectiveness evidence and later an acceptable price is recommended by HIRA through the PE pathway. For clinically non-inferior medicines, an adjusted price is determined by comparing the medicine acquisition costs and recommending the WAP of alternative medicines, based on market share data from reimbursement claims.

However, as noted earlier, providing evidence for PE can be difficult, and there are often limited alternative treatment options for high-cost medicines, particularly those targeting rare diseases or cancers. Hence a series of "alternative P&R pathways", that are different from the traditional route, have been adopted by the South Korean government, as shown in Figure 2 and described below.

Figure 2. Schematic presentation of pricing and reimbursement pathways for new medicines



Adapted from [Lee JH. Pricing and Reimbursement Pathways of New Orphan Drugs in South Korea: A Longitudinal Comparison. Healthcare. 2021; 9(3):296.]

Alternative Pricing & Reimbursement (P & R) pathways

Essential Medicines list

For new medicines that do not have alternative treatments available and for which cost-effectiveness evidence cannot be submitted, the Drug Evaluation Expert Committee (DREC) of HIRA, can list them as essential medicines if they meet the criteria (see Table 1), and it then becomes exempt from requiring a cost-effectiveness evaluation. The price is determined by negotiating with the NHIS based on the adjusted price from seven countries known as A7 countries - US, UK, Italy, Germany, Japan, Switzerland and France.

Risk-Sharing Agreement System (RSA)

RSAs were introduced in 2013 to alleviate the financial burden of accessing high-cost medicines. There are four types of RSAs: 1) **condition treatment continuation and money back guarantee,** which is reimbursed by the payer (NHIS) if the response of a medicine meets a pre-defined goal; if it does not meet the goal, company refunds the full cost to NHIS; 2) **an expenditure cap,** wherein the total expenditure of medicine is set in advance and the company pays back the exceeding amount to NHIS; 3) **a refund** approach, wherein the company refunds a certain percent of the nominal price to the NHIS; and 4) a **utilisation cap,** wherein a fixed cost per patient is agreed upon and the company covers the cost of the medicine beyond the pre-agreed level of utilisation [11].

Pharmaco-economic waiver

Evidence generation for medicines to treat rare and ultra-rare diseases is difficult. To counter this limitation, the PE waiver was introduced in 2015, and only those medicines that satisfy all criteria such as the medicine being used to treat a rare disease (see full list in Table 1) were eligible for this scheme. Later, it was mandated that every medicine for which economic evidence was not generated needed to share the risk in the form of an expenditure cap RSA between the manufacturer and insurer/payer.

Price negotiation waivers

Price negotiation waivers accelerate the process of listing new medicines. If a pharmaceutical company accepts the weighted average price of an alternative medicine (90 or 100 % as in figure 2), it can skip the negotiation process that usually takes 60 days with the NHIS.

For medicines with no alternatives, the average price of the same medicine from the A7 countries is used as a reference price. In this case, an RSA may be applied to spread financial risk related to uncertain clinical usefulness and budget impact. For this reason, these medicines can be listed at high prices through a comparatively simple process [12].

Table 1. Criteria for P&R pathways for medicines with no alternatives

Pathway	Criteria	Comments
Without alternatives		
Essential Medicines	• No alternatives • Treat life threatening conditions • Treat small patient groups • Significant improvement in clinical efficacy or patient survival	• *Life threatening* refers 2 years or less of life expectancy • Unclear definition of *small groups*
Risk Sharing Agreement	• No alternatives • Anti-cancer agent or serious life-threatening diseases • Should be approved via drug review committee on severity, social and ethical influences	• Refund based RSA most used (mandatory PE evidence) • Contract term of 4 years cannot be extended if alternatives exist • No expansion of indications for P&R
Pharmacoeconomic evaluation exemption	• Rare disease and rare cancers • Clinically effective, as proven by single arm RCT or phase II trial. • Medicines to be listed in at least three of A7 countries	• Expenditure cap RSA - with the pharmaceutical sector • Price is based on lowest adjusted list price from A7 countries.
Price negotiation waiver	• If pharmaceutical companies accept the weighted average price, the medicine is exempt from the negotiation process (which can take 60 days)	

Monitoring and Evaluation

Although the mechanism for the Monitoring and Evaluation (M&E) of these schemes has not been reported, the South Korean government has conducted frequent audits for medicines that have been approved under the new alternative pathways programme [13]. As rule of thumb, any medicine approved through

the RSA needs to submit the effectiveness evidence (i.e. no alternative treatment available, improves survival and/or quality of life) every four years in order to be eligible for extension of exemption.

In terms of impact, at HIRA, the Pharmaceutical Benefit Coverage Assessment Committee (PBCAC) meets monthly to review company submissions for medicine reimbursement. PBCAC assesses the suitability of medically essential medicines, RSA, the waiver of PE data submission, and the new mode of action, along with clinical usefulness and cost-effectiveness. Application of new modes of access have shown a positive impact [14] on both listing for reimbursement and time to listing: more than 50% of medicines listed post alternative pathway introduction were cancer and rare disease medicines and the time to listing reduced by approximately 8 months [15]. As of 2019, 39 medicines had been reimbursed under RSAs and PE exemptions had been applied to 19 of these medicines. The impact of alternative pathways on patients was reported in an early analysis of reduced out of pocket expenditure by USD 299.8 million[16]. However, this costed the government approximately USD 75.8 million, with the largest amount for medicines listed under the RSA system followed by PE waiver system, respectively[17].

For the list of essential medicines, since the criteria for listing medicines in the essential category are very specific, the system has so far proven to not be effective when it comes to patient access and as of year 2017, only 10 medicines evaluated by HIRA have been designated as "essential medicines"[17].

Introduction of such schemes have led to increased possibility of listing in the benefit package. Also, a study by Kim S. et al found that the lead time i.e., time taken from market authorisation to an HTA reimbursement decision, was reduced after the introduction of new alternative pathways from median 21 months to 10.9 months. This difference is mainly attributable to pathways such as the price negotiation waiver and PE exemption. However, when RSA individually were evaluated, it took 29.1 months for medicines to be listed and reason reported was additional time to review economic evidence[15, 18].

Conclusion

In conclusion, the introduction of alternative P&R pathways in South Korea has allowed for increased access to high-priced medicines for rare diseases and life-threatening conditions. This has been achieved through risk-sharing agreements and other non-traditional pathways, which waive the need for cost-effectiveness evidence.

However, the increased access to such medicines has led to higher government expenditure and raised concerns around price transparency. Additionally, generating cost-effectiveness evidence for medicines under the refund scheme remains challenging and stakeholders have expressed concerns about producing such evidence (15, 19). Other issues such as high administrative cost, generation of cost-effectiveness evidence for the refund type of evidence continue to pose challenges for both, the payer and the pharmaceutical company(20).

These challenges highlight the need for continued efforts towards finding a balance between access to innovative therapies and cost containment while ensuring transparency and sustainability of the healthcare system.

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