Access to precision medicine in Thailand: a comparative study

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Abstract

Purpose – This study explored health insurance coverage of genetic testing and potential factors associated with precision medicine (PM) reimbursement in Thailand.

Design/methodology/approach – The study employed a targeted review method. Thirteen PMs were selected to represent four PM categories: targeted cancer therapy candidate, prediction of adverse drug reactions (ADRs), dose adjustment and cancer risk prediction. Content analysis was performed to compare access to PMs among three health insurance schemes in Thailand. The primary outcome of the study was evaluating PM test reimbursement status. Secondary outcomes included clinical practice guidelines, PMs statement in FDA-approved leaflet and economic evaluation.

Findings – Civil Servant Medical Benefits Scheme (CSMBS) provided more generous access to PM than Universal Coverage Scheme (UCS) and Social Security Scheme (SSS). Evidence of economic evaluations likely impacted the reimbursement decisions of SSS and UCS, while the information provided in FDA-approved leaflets seemed to impact the reimbursement decisions of CSMBS. Three health insurance schemes provided adequate access to PM tests for some cancer-targeted therapies, while gaps existed for access to PM tests for serious ADRs prevention, dose adjustment and cancer risk prediction.

Originality/value – This was the first study to explore the situation of access to PMs in Thailand. The evidence alerts public health insurance schemes to reconsider access to PMs. Development of health technology assessment guidelines for PM test reimbursement decisions should be prioritized.

Keywords Precision medicine, Genetic test, Access, Reimbursement, Thailand

Paper type Review

Introduction

Precision medicine (PM) is an approach to accurately select treatments or preventive measures based on the individual patient's genetic information. The human genome project

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was first initiated in 1990 [1]. Since then, the knowledge in this field has greatly expanded. The Precision Medicine Coalition reported that the market authorization of genetic testing has sharply increased during the past decade [2]. As of 2019, there were more than 187 biomarkers for 377 companion drug items registered with the US FDA [3, 4]. Although knowledge about PM has been very well established for years, the adoption of PMs in clinical practice is still limited in many countries [5, 6].

Unlike their companion drugs, PM testing did not have a clear health technology assessment (HTA) framework for reimbursement decisions. In 2009, Meckley and Neumann explored factors affecting the reimbursement of six PMs in four public and private health insurers in the United States and the National Health Service of the United Kingdom. They found that the strength of clinical evidence synergized with the availability of clinical guidelines was a strong predictor of PM reimbursement decisions. On the contrary, types of PM test's regulatory and cost-effectiveness analysis were not associated with the reimbursement decision [7].

Chong *et al.* described the adoption of PMs among four Southeast Asian countries using five proxy PMs. They found that the countries did not have 1) a national strategic plan, 2) a comprehensive PM legislation, 3) a PM legal framework, and 4) PM data management system. Although these countries had an official HTA body, they did not have PM test-specific HTA guidelines [8].

In Thailand, neonatal screening for congenital hypothyroidism, phenylketonuria and thalassemia was initiated in 1992-1993 [9–11]. Presently, there are several ongoing PM research projects potentially applicable for targeted cancer drug selection, cancer risk prediction, rare diseases identification, severe adverse drug event prevention and drug metabolite prediction [12–15]. The majority of the genetic tests were provided free under research studies or as an ad hoc project. In 2013, the Health Intervention and Technology Assessment Program (HITAP) conducted an economic evaluation of *HLA-B*15:02* and suggested that universal *HLA-B*15:02* screening was cost-effective in preventing Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) in neuropathic pain patients treated with carbamazepine but was not cost-effective for epileptic patients [16]. The result, however, depended on the accuracy of the prevalence input in the economic model. The Department of Medical Sciences, in the same year, launched a project to provide *HLA-B*15:02* screening tests in the Bangkok area. The pilot project aimed to lessen carbamazepine-induced severe cutaneous adverse reactions (SCARs). In 2016, the project was expanded to other provinces and covered two additional genetic tests; *HLA-B*57:01* and *HLA-B*58:01* [17]. Thailand has 24 medical geneticists but does not have genetic counselors [5, 8]. The Pharmacogenetic ID card was developed and provided to patients who had undergone genetic tests to ensure patient safety [18]. Furthermore, a basic pharmacogenetics course is taught in both medical school and pharmacy school, but only for a few hours [19–23]. Genotyping laboratory services were available, but only in some government laboratory and super-tertiary hospitals, for example, in 15 centers of the Department of Medical Sciences and six university hospitals [24].

The Thai healthcare system is recognized internationally. All Thai citizens are covered under one of the three mandatory public health insurance schemes: (1) Civil Servant Medical Benefit Scheme (CSMBS) for government staff and their dependents, (2) Social Security Scheme (SSS) for private-sector workers and (3) Universal Coverage Scheme (UCS) for those not eligible for the CSMBS or SSS schemes. The CSMBS, SSS and UCS covered 7.73%, 18.84% and 70.75% of the Thai citizens, respectively [25]. All schemes provide a comprehensive package, including outpatient visits, hospital admission, accidental and emergency services, pharmaceutical benefits, x-ray and laboratory testing.

All three schemes use a similar payment mechanism for in-patient services. UCS and CSMBS use diagnostic related groups (DRGs) with global budget payment, while SSS uses a combination of capitation and DRG with global budget payment. Drug, x-ray and laboratory testing are bundled with doctor visits under capitation payment. The CSMBS, on the other hand, uses per-item payment for pharmaceutical benefits and has a fee schedule for x-ray and laboratory testing [26, 27].

Although Thailand has a good performance of their health insurance system, inequity among the three public health insurers was observed. Patikorn *et al.* found that access to high-cost anti-cancer drugs was better among CSMBS than among SSS and UCS [26]. Sermsri *et al.* also confirmed the disparity of treatment choice among colorectal cancer patients in the CSMBS vs UCS schemes, thus resulting in a gap in treatment outcome [27].

The majority of the existing research in Thailand focuses on gene-disease association and the development of genetic testing methods. Very little attention has been paid to explore access to PM tests. This study intended to explore Thailand's health insurance coverage of PMs, especially genetic testing, among the three public health insurance schemes in Thailand. Potential factors associated with PM reimbursement were also explored.

Methods

This study utilized a targeted review method to evaluate patient access to PMs and explore factors that might be associated with PM testing reimbursement among three health insurance schemes in Thailand. Thirteen biomarkers were selected as a representative of four PM categories: (1) PM for targeted cancer drug selection, (2) PM for the prediction of drug-induced SCARs, (3) PM for dose adjustment and (4) PM for cancer risk prediction. The basic characteristics of the 13 PMs are described in Table 1. The price range of the selected PM testing was very high in the *BRCA1/2* gene (19,400–50,000 Thai baht), compared to 1,100–11,000 Thai baht for other PM categories.

The framework of this study was adapted from Meckley and Neumann [7], which was composed of four variables: PM test reimbursement status, genetic test mentioning in clinical practice guidelines, genetic test information in drug labeling and value for money of the genetic test. Reimbursement status was determined as "Yes" only when reimbursement evidence was clearly stated in the official documents. Genetic test information in drug labeling was classified into three categories: "required," "recommended," and "informative." "Required" was assigned when genetic testing was stated or indicated necessary in drug labeling. "Recommended" was specified when drug labeling stated that genetic testing should be provided or performed. "Informative" was used when drug labeling provided information to educate readers. This study explored guidelines endorsed or created by the Royal College of Thai Physicians, and the results of the economic evaluation of PMs in the context of Thailand.

A comprehensive search was conducted in PubMed to identify relevant economic evaluation articles related to the 13 selected PMs in Thailand. Search terms included "(Name of genetic biomarkers) AND Thailand." Furthermore, the official websites of government organizations, insurers, national HTA organizations, and healthcare professionals were searched to ensure the completeness of information. The targeted search was conducted up until February 29, 2020. The language was limited to Thai and English. Content analysis was performed to compare access to PMs among CSMBS, SSS, and UCS in four aspects: reimbursement status, clinical practice guideline, statement in an FDA approved leaflet and economic evaluation results.

Ethical issue: Review paper do not need approval code

Precision medicines					
Biomarker	Companion drug/Therapy	NLEM status of drug [28]	Benefits of PM tests	Therapeutic area	Price of PM tests* (2020 Thai baht)
PM for targeted cancer drug selection					
HER2/neu	Trastuzumab	NLEM	Trastuzumab candidate	Oncology	10,000
BCR-ABL	Imatinib	NLEM	Tyrosine kinase inhibitors candidate	Oncology	1,100–6,000
	Nilotinib	NLEM		Oncology	
	Dasatinib	NLEM		Oncology	
EGFR mutation	Gefitinib¶	Non-NLEM	EGFR inhibitors candidate	Oncology	7,000–11,000
	Erlotinib¶	Non-NLEM		Oncology	
PM for the prediction of drug-induced SCARs					
*HLA-B*15:02*	Carbamazepine	NLEM	Prevent drug-induced SJS/TEN	Neurology	1,000–2,000
*HLA-B*57:01*	Abacavir	NLEM	Prevent drug-induced HSR	Infectious diseases	1,000–2,000
*HLA-B*58:01*	Allopurinol	NLEM	Prevent drug-induced SJS/TEN	Rheumatology	1,000–2,000
PM for dose adjustment					
TPMT	Azathioprine	NLEM	Predict azathioprine-related bone marrow toxicity	Rheumatology	1,800–3,400
UGT1A1	Irinotecan	Non-NLEM	Predict irinotecan-related toxicity	Oncology	1,400–1,700
CYP2C19	Clopidogrel	NLEM	Monitoring response to clopidogrel therapy	Cardiology	1,800–3,500
CYP2C9	Warfarin	NLEM	Adjust warfarin dosing	Hematology	1,000–2,000
VKORC1	Warfarin	NLEM	Adjust warfarin dosing	Hematology	2,950
CYP2D6	Tamoxifen	NLEM	Monitor tamoxifen efficacy	Oncology	1,800–4,800
PM for cancer risk prediction					
BRCA1/2	Breast cancer monitoring/ mastectomy		Assess risk of breast or ovarian cancer development	Oncology	19,400–50,000

Note(s): ¶ = Drug not listed in the National List of Essential Medicine (NLEM) but reimbursed under the CSMBS Oncology Prior Authorisation (OCPA) list
* = Published price list from Chulalongkorn Memorial Hospital, Ramathibodi Hospital and Siriraj Hospital [29–31]
Abbreviations: HSR; hypersensitivity reactions, NLEM; national list of essential medicines of Thailand, PM; precision medicine, SCARs; severe cutaneous adverse reactions, SJS/TEN; Stevens-Johnson syndrome/toxic epidermal necrolysis

Table 1.
Characteristics of 13 studied precision medicines

Results

Reimbursement status of the selected precision medicines

The reimbursement status of the selected PMs across the three public health insurance schemes in Thailand is summarized in Table 2. Overall, CSMBS patients have access to 10 out

Precision medicine test Biomarker	Reimbursement status CSMBS	SSS	UCS	Clinical practice guideline International	Thai	Statement in FDA approved leaflet	Economic evaluation results
PM for targeted cancer drug selection							
HER2/neu	Yes [32]	Yes [33]	Yes [34]	NCCN2020 [35], ESMO2019 [36]	NCI 2017 [37]	Required	Cost-effective [38]*
BCR-ABL	Yes [32]	Yes [33]	Yes [34]	NCCN2020 [39], ESMO2017 [40]	ThaiCML 2011 [41]	Required	Cost-effective [42]*
EGFR mutation	Yes [32]	No	No	NCCN2020 [43], ESMO2018 [44]	NCI 2015 [45]	Required	Cost-effective [46]
PM for the prediction of drug-induced SCARs							
*HLA-B*15:02*	Yes [47]	No	Yes [48]	CPIC2018 [49], CPNDS2014 [50]	Thai epilepsy society 2011 [51]	Required	- Neuropathic pain: cost-effective - Epilepsy: Not cost-effective [16]
*HLA-B*57:01*	Yes [52]	No	No	WHO2016 [53], CPIC2012 [54], DPWG2019 [55]	Thai AIDS society 2017 [56]	Recommended	Study not found
*HLA-B*58:01*	Yes [47]	No	No	ACR2012 [57], CPIC2013 [58]		Recommended	Cost-effective [59]
PM for dose adjustment							
TPMT	Yes [47]	No	No	CPIC2018 [60], DPWG2019 [61]		Informative	Study not found
UGT1A1	No	No	No	NCCN2020[[62]), DPWG2018 [63]		Informative	Study not found
CYP2C19	Yes [47]	No	No	ACCF/AHA/SCAI2011 [64], ACCF/AHA/ACP/ AATS/ PCNA/SCAI/ STS2012 [65], CPIC2013 [66], DPWG2018 [67]	Thai heart 2014 [68]	Informative	Study not found
CYP2C9	Yes [47]	No	No	CPIC2017 [69], DPWG2018 [70], CPNDS2015 [71]	Thai heart 2014 [68]	Informative	Non cost-effectiveness [72]
VKORC1	No	No	No	CPIC2017 [69], DPWG2018 [73], CPNDS2015 [71]		Informative	Non cost-effectiveness [72]
CYP2D6	No	No	No	CPIC2018 [74], DPWG2018 [75], CPNDS2019 [76]		Informative	Study not found
PM for cancer risk prediction							
BRCA1/2	Yes [47]	No	No	NCCN2018 [77], ESMO2016 [78]		–	Study not found

Note(s): * = companion drug and PM test were bundled when conducting economic analysis
Abbreviations: ACCF: American College of Cardiology Foundation, ACR: American College of Radiology, AHA: American Heart Association, CML: chronic myeloid leukemia, CPIC: Clinical Pharmacogenetics Implementation Consortium, CPNDS: Canadian Pharmacogenomics Network for Drug Safety, CSMBS: Civil Servant Medical Benefit Scheme, DPWG: Dutch Pharmacogenetics Working Group, ESMO: European Society for Medical Oncology, FDA: Food and Drug Administration, NCCN: National Comprehensive Cancer Network, NCI: National Cancer Institute, SCAI: Society for Cardiovascular Angiography and Interventions, SCARs: Severe cutaneous adverse reactions, SSS: Social Security Scheme, UCS: Universal Coverage Scheme, WHO: World Health Organization

Table 2.
Reimbursement status, clinical practice guideline, economic evaluation findings and information in the leaflets of 13 PMs

of 13 tests (77%), followed by 3 tests for UCS patients (23%) and 2 tests for SSS patients (15%). The companion drugs of the selected PMs were mostly listed in the National List of Essential Medicines (NLEM) of Thailand except for gefitinib, erlotinib and irinotecan. The NLEM drugs were reimbursable for patients in all insurance schemes. However, CSMBS patients can still access non-NLEM drugs previously mentioned through different channels such as the OCPA program or prescribing criteria for non-NLEM drugs.

Among four PM types, PM for targeted cancer drug selection was more likely to be reimbursed by all schemes. All three tests (100%) were reimbursed by CSMBS, while two tests (67%) were reimbursed by UCS and SSS. The reimbursement status of three pharmacogenetic tests for the prediction of drug-induced SCARs was positive among all three tests (100%) for CSMBS, followed by one test (33%) and none (0%) for UCS and SSS. Three out of six (50%) pharmacogenetic tests for dose adjustment purpose were reimbursed only by CSMBS, while none of them was reimbursed by UCS and SSS. The cancer risk prediction, namely the *BRCA1/2* gene, was reimbursable only for CSMBS patients. It is worth noting that the purpose of PMs may somehow be associated with the reimbursement decision.

Factors associated with precision medicine reimbursement

The possible association was observed across PM types and insurance schemes. The results were described in the following three topics.

Clinical practice guideline. All selected PMs across the four categories were recommended in the international guidelines. However, only five PMs were recommended in the Thai guidelines including three PMs for targeted cancer drug selection (*HER2/neu*, *BCR-ABL* and *EGFR* mutation) [37, 41, 45], and two PMs for the prediction of drug-induced SCARs (*HLA-B*15:02* and *HLA-B*57:01*) [51, 56]. Furthermore, the Thai guideline mentioned about two biomarkers for dose adjustment for warfarin therapy (*CYP2C9* and *VKORC1*) [68]. There was no local guideline for the other six PMs. Out of six Thai clinical practice guideline-recommended PMs, the reimbursable status was positive in five tests for CSMBS (100%), followed by three tests for UCS (60%) and two tests for SSS (40%).

Statement in the FDA-approved leaflet. The statements in the FDA-approved leaflet were found to be "Required" in three PMs, "Recommended" in two PMs and "Informative" for seven PMs. The two reimbursable tests were "Required" for SSS. Out of three reimbursable tests for UCS, two tests were "Required," and one test was "Recommended." None of the "Informative" PMs were reimbursable for UCS and SSS. For CSMBS, all of the PMs with a statement in the FDA approved leaflet as either "Required" or "Recommended" were reimbursable. However, four out of seven "Informative" PMs were reimbursable. In contrast, the *BRCA1/2* gene had no stated information in any FDA-approved leaflet's medicine because both biomarkers were not directly paired with any medicine.

Economic evaluation. Economic evaluation studies were conducted in Thailand assessing six PMs including *HER2/neu* [38], *BCR-ABL* [42], *EGFR* mutation [46], *HLA-B*15:02* [16], *HLA-B*58:01* [59] and *CYP2C9* [72]. All of these studies showed that the use of PMs was cost-effective with the exception of the test for *HLA-B*15:02* in epilepsy patients planning to start carbamazepine to prevent drug-induced SJS/TEN [16], and test for *CYP2C9* to adjust warfarin dosing [72]. Among five cost-effective PMs, the reimbursement status was positive in five tests for CSMBS (100%), followed by three tests for UCS (60%) and two tests for SSS (40%). On the other hand, out of two cost-ineffective PMs, the reimbursement status was positive for two tests for CSMBS patients, followed by one test for UCS and none for SSS.

Discussion

This was the first study to explore the situation of access to PMs in Thailand. The selected PM tests covered 13 out of 50s biomarkers from 4 PM categories. Compared to previous

studies that evaluated access to PMs in the USA, the UK [7] and four Southeast Asian countries [8], this study covered more PM items.

It is still unclear how PM testing was listed in three health insurance benefits packages. However, the reimbursement seemed to favor PMs with drug selection and serious ADR prevention purposes. Among drug selection purposes, PM test reimbursement status was highly associated with its companion drug reimbursement status. Economic evaluation results seemed to impact drug selection, thus indirectly influencing access to companion PM testing for drug selection purposes. It is quite clear in this case that economic evaluation might be a major factor driving the reimbursement decision of both genetics testing and its companion drug in Thailand. However, the factor influencing the reimbursement decision in Thailand was different from the factors found in the United States and the United Kingdom. The strength of clinical evidence and the availability of clinical guidelines strongly predicted the reimbursement decisions of PMs, while the regulatory status and economic evaluations were not [7].

The reimbursement decision of PM testing for the prediction of drug-induced SCARs was unclear. In 2009, several studies reported higher carbamazepine-induced SJS/TEN incidents among more Asians than Caucasians. Later, Tassaneeyakul *et al.* confirmed that Thais had a very high risk of carbamazepine-induced SJS/TEN. The study recommended that the *HLA-B*15:02* should be screened before starting carbamazepine [79]. The government expressed their concern related to pharmacogenetic by launching the first pilot project for *HLA-B*15:02* testing among patients initiating carbamazepine in 2013. Later, the project was expanded to cover more hospitals and two more pharmacogenetic tests: *HLA-B*57:01* for abacavir and *HLA-B*58:01* for allopurinol. It took about five years to list *HLA-B*15:02* for epilepsy patients initiating carbamazepine in the UCS benefit package. Six months later, UCS expanded the coverage of *HLA-B*15:02* for carbamazepine among patients suffering from neuropathic pain [48, 80]. The reimbursement decision was contradicted with the economic evaluation result as *HLA-B*15:02* was not cost-effective for epilepsy but cost-effective for the neuropathic pain subgroup [16].

Although *HLA-B*58:01* was included in a pilot project since 2016 and the cost-effectiveness result was confirmed [59], the decision to include *HLA-B*58:01* was not reached. At least two actions – (1) adding information about the association between *HLA-B*58:01* and SCARs in the product leaflet and (2) inclusion of febuxostat as a restricted benefit in the NLEM list D – were taken to prevent severe ADR in a mean time [28]. Febuxostat was restrictively prescribed only when patients were *HLA-B*58:01* positive.

Furthermore, an increasing trend of Abacavir use was observed. Abacavir was listed D in NLEM as a combination drug to treat HIV patients since 2019 [81, 82]. Abacavir was the only drug in the nucleoside reverse transcriptase inhibitor (NRTI) category not requiring dose adjustment in patients with renal impairment [56]. *HLA-B*57:01* testing before prescribing Abacavir was recommended by several practice guidelines, both internationally and domestically. Moreover, the Thai FDA also recommended in the leaflet that patients should take an *HLA-B*57:01* test before using Abacavir. Although *HLA-B*57:01* was included in a phase II pharmacogenomic pilot project since 2016, at the time of conducting this research, SSS and UCS had not yet included it in their benefits packages. One possible explanation was the incidence of serious ADR was low among Asian people [56]. This evidence corresponded to previous studies that showed that the prevalence of *HLA-B*57:01* was found at a lower rate among Chinese, Thai and Cambodian people compared to Europeans [83, 84].

It was unlikely that insurers supported biomarkers with dose adjustment purposes. In general, patients taking drugs such as warfarin should have regular clinical monitoring. *CYP2C9* and *VKORC1* were mentioned in the clinical guideline as they are pharmacogenetic makers that are highly associated with warfarin metabolism. This information, however, was not translated into a strong recommendation in the FDA-approved leaflet. One possible explanation was that regardless of the existing genes, the doctors should still closely monitor

INR and ADR among patients receiving warfarin [68]. The economic evaluation also confirmed that *CYP2C9* and *VKORC1* were not cost-effective [72].

BRCA1/2 was reimbursed only under CSMBS. Treatment options like mastectomy and salpingo-oophorectomy need not only patients' understanding and involvement [85, 86], but also financial coverage from health insurers when patients decide to undergo those surgeries to prevent breast and ovarian cancer [87].

The costs of PM testing for targeted cancer drug selection were not solely covered by the three health insurance schemes, especially for non-NLEM drugs. Patikorn *et al.* also found that the costs of PM testing for targeted cancer drug selection were also covered by pharmaceutical companies under Patient Assistance Programs (PAPs) such as the *HER2/nue* gene for trastuzumab and *EGFR* mutation for gefitinib [26]. This strategy was probably done with the intention to mitigate the costs of PM tests from both the healthcare providers and patients.

As this study utilized the document review method, the result reflected only the official PM coverage policy obtained from official documents which was considered a major limitation of the study. First, access to PMs in real practice might be deviated from official announcements due to the differences in healthcare financing mechanisms of the three health insurance schemes, especially for SSS and UCS. Doctors could order PM tests to ensure patient safety. Although PMs were not listed in the benefits package, their expenditure would be absorbed by the hospitals under the capitation payment scheme. Unlike CSMBS, PMs were reimbursed only if they were in the benefits package and paid for under the per item payment system. If doctor-prescribed PMs are not listed in the benefits package, CSMBS patients are required to pay out of their own pocket. It could be implied that under some circumstances, healthcare professionals might be reluctant to provide PM tests for patients in need, especially those under UCS and SSS, because there is no clear list of reimbursable tests. Second, the factors found to likely influence the reimbursement decisions in this study were based on a retrospective review of literature and government documents. Under some circumstances, the reimbursement decisions might not be made based on either the statement in FDA approved leaflets or the economic evaluation results.

With the previously mentioned limitation, additional in-depth interviews with healthcare professionals, payers and policymakers are recommended for future research to explore practice variation, perspective on PMs and reimbursement decisions framework. PMs are well known among healthcare professions in Thailand; however, very little was known about the general people's perception. The payers or responsible organizations in Thailand should consider formulating not only HTA guidelines specific to PM tests but also develop a reimbursement list of PM tests. PM tests that are proven to be valuable for the health system should be unbundled from the capitation payment scheme to increase access to PM tests for the Thai population. Patients should also be empowered and be able to communicate risks associated with their existing genetics to their doctors to ensure safe drug administration. Patient education about PM is needed.

Conclusion

The study showed that there was a discrepancy in access to PMs among the three public health insurance schemes in Thailand. CSMBS is the most generous scheme compared to SSS and UCS in providing their beneficiaries the access to PMs. Three health insurance schemes provided adequate access to PM tests for some cancer-targeted therapies, while gaps existed for access to PM tests for serious ADRs prevention, dose adjustment and cancer risk prediction. Clinical practice guidelines may not be considered factors associated with PM reimbursement status as the major aim is to provide educational information. Although local clinical guidelines were not available for all drug biomarkers, healthcare professionals normally refer to the international guidelines. Statements in the FDA-approved leaflet, which are indicated as "required" and "recommended," seemed to have an impact on the

reimbursement status of CSMBS, while "required" likely impacted the reimbursement status of SSS and UCS. Economic evaluation seems to influence PM reimbursement decisions of SSS and UCS, while CSMBS reimbursed PMs regardless of economic evaluation results. However, there was no specific HTA guideline. It is therefore suggested that PM-specific HTA guidelines should be established.

Conflict of Interest: None

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