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PERSPECTIVE

Importance of aligning the implementation of new payment models for innovative pharmaceuticals in European countries

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ABSTRACT

Introduction: The uptake of complex technologies and platforms has resulted in several challenges in the pricing and reimbursement of innovative pharmaceuticals. To address these challenges, plenty of concepts have already been described in the scientific literature about innovative value judgment or payment models, which are either (1) remaining theoretical; or (2) applied only in pilots with limited impact on patient access; or (3) applied so heterogeneously in many different countries that it prevents the health care industry from meeting expectations of HTA bodies and health care payers in the evidence requirements or offerings in different jurisdictions.

Areas covered: This paper provides perspectives on how to reduce the heterogeneity of pharmaceutical payment models across European countries in five areas, including 1) extended evaluation frameworks, 2) performance-based risk-sharing agreements, 3) pooled procurement for low volume or urgent technologies, 4) alternative access schemes, and 5) delayed payment models for technologies with high upfront costs.

Expert opinion: Whilst pricing and reimbursement decisions will remain a competence of EU member states, there is a need for alignment of European pharmaceutical payment model components in critical areas with the ultimate objective of improving the equitable access of European patients to increasingly complex pharmaceutical technologies.

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Affordability; alternative access schemes; complex technologies; evaluation framework; innovative pharmaceuticals; payment model; value judgment; uncertainty

1. Introduction

Until the turn of the millennium pharmaceutical R&D focused mostly on the development of small molecules for acute and chronic diseases. The payment model for these relatively low-cost medicines in outpatient care was fairly simple, mainly positive drug listing with payment at use was applied by health care payers. As described in Figure 1, in recent periods, the focus of pharmaceutical R&D moved away from primary care therapies to fairly complex technologies in special diseases with high unmet medical need and often with relatively small patient populations [1].

The uptake of new technological platforms, such as combinations of personalized biopharmaceuticals with diagnostics or digital health solutions, mRNA vaccines, or cell and gene therapies that are manufactured for individual patients, has resulted in several challenges in the pricing and reimbursement of innovative pharmaceuticals.

First, the production and administration costs of several new technologies have become significantly more expensive than previous small-molecule medicines [2].

Second, the adaptation of regulatory requirements for priority medicines (e.g. orphan drugs), the growing public health attention to preventive medicines (e.g. vaccines), and the increasing R&D focus on single-use technologies with long-term effects (e.g. potentially curative advance therapy medicinal products – ATMPs) is associated with limited evidence at the time of initial regulatory approval on long-term efficacy and safety [3–5]. This is especially true in the context of schemes that provide early access to such promising technologies. The uncertainty in judging the precise clinical value of these technologies creates confusion in calculating the value-based price in different jurisdictions.

Third, for combined technologies, including combinations of i) drug and drug, ii) drug and device, iii) diagnostic and drug, and iv) drug and digital health application, complex pricing arrangements have become necessary. The co-dependence of different components on delivering expected benefits in the real world, and the uncertainty in adherence to recommended use, – for example whether health care professionals and patients apply the diagnostic, device, or digital component appropriately – cannot be evaluated appropriately in the current standard single technology appraisal process, which makes it difficult for policymakers to link the true value of combined health technologies to a fixed price [6].

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Article highlights

- The uptake of complex technologies and platforms has resulted in several challenges in the pricing and reimbursement of innovative pharmaceuticals.
- To address these challenges, several new payment models for special innovative pharmaceutical technologies have been described in the scientific literature.
- Apart from financial managed entry agreements, novel payment model components are applied only in pilots with limited impact on patient access or applied heterogeneously in different countries.
- If changes in payment model components and related value judgment methods go into different directions in EU member states, multinational pharmaceutical companies may not be able to generate a truly global value proposition and supportive evidence package, which is uniformly acceptable in the majority of countries.
- The highest need is not the design of additional novel payment models, but the uptake and more aligned use of previously piloted payment model components in EU member states. The paper outlines the vision of the authors on the five most important areas for harmonized actions in the European Union.

Fourth, the development of innovative technologies is currently dominated by large pharmaceutical companies and/or small biotech companies that may be funded by venture capitalists [7]. These companies have become dependent for their profits on the use of their technologies either in areas with public health need (such as infectious diseases, e.g. Hepatitis C, COVID-19) or in small patient populations, leading to very high prices [8,9]. Recently, the development phase and pre-clinical research of new health technologies have often been supported by public funding [10]. Continued public funding through the clinical research phase may ensure that new technologies can reach patients with more affordable and sustainable prices [11]. As countries and public entities are exploring additional processes for the development of new technologies partially or dominantly from public resources [12], guidance is needed on how public investment should be taken into account in current payment models [13].

Some of these changes already started 20 years ago, such as the introduction of biological medicines with more complex manufacturing process, regulatory incentives through exemptions to orphan medicines, combination of molecular diagnostics and medicines in targeted therapies, or public–private partnership in the development of medicines with high unmet medical need. However, in recent years, these factors become the new norm in pharmaceutical innovation, more and more pharmaceuticals are manufactured for individual patients, combination of technologies has been further extended to medicines, diagnostics, and digital health solutions, the adaptive regulatory pathway is applied to more technologies, and public institutes are increasingly participating in the R&D process. Finally, there is a trend to move away from a supply-side approach to pharmaceutical R&D, in which pharmaceutical companies decide on which therapies to develop for which diseases, toward a demand-side approach, in which public policy-makers determine which therapies are needed and how much they are willing to pay for them.

Health care professionals and patients have fair expectation to access and apply these complex health technologies, which have been launched with increasingly high price tags. In fact, developments in pharmaceutical technologies are fast-moving and outpace the growth rate of health care budgets. The difficulties around valuing highly priced medicines with partially uncertain effects challenge the sustainability of health care financing and equitable patient access across and within countries all over the world, and increase insecurity in various communities, including patients. This necessitates the reconsideration of payment models.

To address these challenges for special innovative pharmaceutical technologies in the short- and mid-term, several new payment models have been described in the scientific literature and experimented with through pilot cases in different countries [14]. However, apart from financial-based risk-sharing agreements (RSAs), the uptake of other new payment models (e.g. performance-based RSAs) is relatively slow, unpredictable, and heterogeneous in European countries, which puts pressure on the global healthcare industry in generating a truly global value proposition and supportive evidence package, which is uniformly acceptable in the majority of countries. Designing and implementing heterogeneous market access strategies for innovative medicines in European countries result in unnecessary challenges and inefficiencies for pharmaceutical manufacturers. This paper provides perspectives on how to reduce heterogeneity of pharmaceutical payment models across European countries with the ultimate objective of improving the equitable access of European patients to innovative medicines.

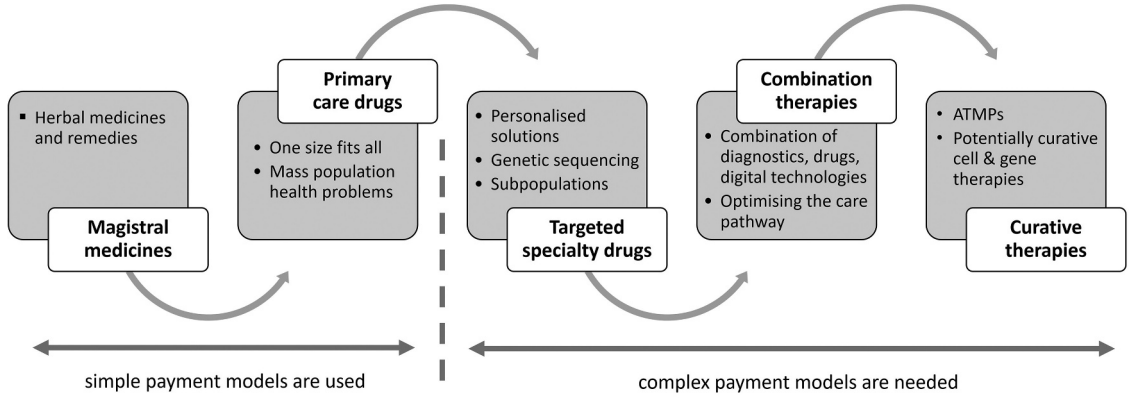

Figure 1. Implications of pharmaceutical R&D trends on payment models.

2. Priority areas for improvement

Payment models for pharmaceutical technologies consist of fundraising, pooling, and resource allocation elements, as illustrated in Figure 2. In European countries, health care financing is mostly based on solidarity principles and community-rated fundraising techniques (such as taxes or public health insurance premiums). Although the expectation that each EU member state should spend more of their growing GDP and wealth on health versus other priorities is a necessary practical and ethical need, to maintain and improve equity in healthcare financing in European countries, new payment models for high-cost pharmaceutical technologies should be in line with the boundaries of public health care budgets. Alternative fundraising or pooling methods based on voluntary health insurance or community-based approaches cannot be the primary solution for ensuring patient access to new technologies in the European health care systems in the next periods. As such, the scope of innovative payment models in European countries should not focus on the full spectrum of healthcare financing, but improve alignment in the four components of resource allocation (see Figure 2).

The first component is about how the value of new technologies is judged in patient-centered and societally oriented health care systems, and how the value judgment contributes to the price setting of new medicines. The second component is the choice on the financing route, including joint international procurement, central procurement, reimbursement, institutional financing, and reimbursement on a named patient basis. The third component may set conditions (e.g. financial, or performance-based risk-sharing agreements) or restrictions (e.g. only second-line use or prescription only in selected centers) for public payments. Timing of payment is the fourth component with more strategic and predictable use of delayed or spread payment models. There is no need for all components in each payment model, e.g. novel payment models can be implemented without the value assessment component or conditions to reduce uncertainty

We here outline our vision on which are the five most important areas for harmonized actions related to the uptake of previously piloted payment model components in the European Union.

2.1. Area for harmonized action #1: need for extended evaluation frameworks to judge the value of new technologies

Defining value in health care, and more specifically value of medicines, although extensively studied, still represents a challenge [15]. Inconsistency in capturing the full spectrum of added value results from value components, perspective, and scope [16]. Value-based prices of new technologies are usually determined by national HTA bodies based on traditional evaluation frameworks. These traditional HTA frameworks have been focusing on health gain and incremental health care costs, which may not capture improvements in patient-centricity of pharmaceutical care [17], broader societal benefits, or environmental aspects according to the European Green Deal.

Even if some technologies (i.e. ATMP) or therapeutic areas (i.e. rare, or infectious diseases) fuel the need for more comprehensive and multidimensional value assessment, several countries are resistant to move away from traditional frameworks, which have been observed to be fairly useful in the pricing and reimbursement process of medicines in common diseases for many years. On the other hand, the extension of evaluation frameworks has started in certain jurisdictions for some technologies, such as orphan medicines [18], the additional value criteria are selected and measured heterogeneously across countries. Countries differ not only in the uptake and acceptance of additional value elements but also in the way of how they are taken into account in policy decisions. Although multicriteria decision analyses (MCDAs) or augmented cost-effectiveness analyses (ACEAs) [19] were experimented with in some countries, it has not replaced less transparent and less predictable approaches to aggregate different value elements in policy decisions in the majority of countries [20]. Simultaneously, many countries have implemented some form of adaptive reimbursement processes for certain types of drugs (e.g. orphans or conditionally approved products), but these adaptive reimbursement processes are not in line with one another.

Without more clarity on whether and which additional value elements are taken into account, how they are defined, how they should be measured, and how they are considered

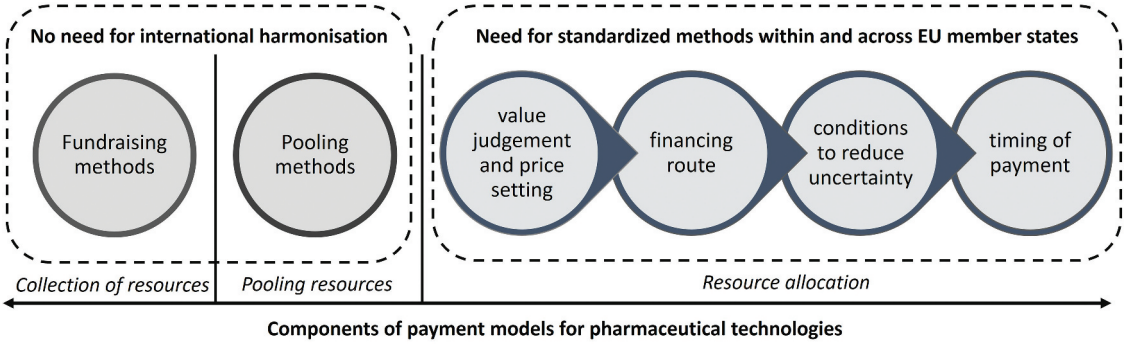

Figure 2. Recommended scope of international harmonisation for pharmaceutical payment models in EU countries.

or aggregated in judging the full value of medicines in different countries (especially with significant market potential), there is no general guidance to technology developers on how to generate scientific evidence for extended evaluation frameworks in the development phase to justify the value-based price at product launch. Although EUnetHTA joint actions were promising steps toward harmonizing the value assessment of health technologies across EU member states, the subsequent EU HTA regulation does not provide a solution to reduce the heterogeneity of selecting additional value criteria, as it focuses only on joint clinical assessments. While it is unlikely to reach a single extended value assessment methodology for all EU member states in the near future, even reduced heterogeneity of evaluation frameworks to limited country archetypes would be beneficial for all stakeholders.

2.2. Area for harmonized action #2: uncertainty in the benefits of new pharmaceutical technologies in health care financing

In recent years, plenty of publications have described how uncertainty in the clinical value can be improved by implementing payment models with performance-based RSAs [14,21], and how evidence generated in such agreements should be shared with health care professionals and patients, if scientific evidence of new technologies is considered a global public good [22]. Several countries apply other terms for risk-sharing agreements, such as managed entry agreements (MEAs) or patient access schemes (PASs), especially if the primary objective of these agreements is confidential price reduction.

It must be noted that some EU countries have experimented with different types of performance-based RSAs, out of which the Italian example coordinated by AIFA has been the most comprehensive approach [23]. As there are practical challenges with implementing performance-based RSAs, most countries to this day rely mainly on financial-based RSAs due to their administrative simplicity [24,25]. However, financial schemes do not incentivize the collection of the necessary data to resolve clinical and economic uncertainties or ensure that the risks to patients or the healthcare system are managed. With the early predicted uptake of adaptive regulatory pathways for ultra-orphan medicines, vaccines, potentially curative cell and gene therapies through conditional market approvals, and in general more complex technologies, the need for addressing clinical uncertainty in temporary payment models (applied before the final market authorization) should be reconsidered [26]. Therefore, European framework on the design and implementation of performance-based RSAs is much awaited.

As more and more clinical data are digitalized and collected consistently in a standardized format, as is conceptualized in the proposal of the EU on the European Health Data Space (EHDS), there is hope to effectively mitigate the administrative barriers of generating real-world evidence; thus, in theory, broader implementation of performance-based RSAs should be facilitated [27]. Real-world health outcomes may be impacted by local clinical practice and health system arrangements, thus corresponding uncertainty needs decomposition on technology-related and other determinants of clinical outcomes. Appropriate quantitative methods play a key role in the assessment of outcomes in real-world settings. Consequently, the analysis of clinical outcomes also needs European good practices statements, which should cover differences in local health care arrangements, especially in countries with restricted reimbursement and hidden access barriers compared to registered indications [28].

2.3. Area for harmonized action #3: inefficient value judgement and price negotiation procedure for technologies with high unmet medical need and (1) low volume or (2) urgency

Pooled procurement across countries has the potential to improve the administrative efficiency and facilitate more affordable prices by increased economies of scale, which is especially needed when individual countries have to negotiate about low volumes (e.g. in ultra-rare diseases) or when they are under time pressure (e.g. in the case of pandemic periods). With respect to low-volume medicines, several multi-national pooled procurement initiatives exist, such as the Beneluxa Initiative, the Nordic Pharmaceuticals Forum, the Baltic Procurement Initiative, and the Valletta Declaration. However, these initiatives have different remits, have to address differences in legislations and processes in participating countries, and perform diverse activities (in addition to pooled procurement). Also, to date, pharmaceutical industry has shown limited interest in collaborating with these initiatives [29]. With respect to urgent technologies, the example of purchasing and paying for vaccines in the context of the COVID-19 pandemic has highlighted benefits and difficulties of securing sufficient doses for EU citizens in addition to problems with inequitable supply to countries outside the European Union, vaccine nationalism, and over-spending by some countries. The joint EU procurement of COVID vaccines provides an important reference case about the complexities of international collaboration in forecasting supply and needs and implementing equitable pricing and procurement models [30].

Based on experiences from reference cases, future pooled procurement initiatives should be implemented by taking into account important principles. First, participation in such initiatives should be initiated by the voluntary decision of individual countries or payer organizations. In the long run, mandatory and legislative processes may be necessary to ensure more consistent and structural approaches to joint procurement. Especially large countries may see less benefits from helping smaller countries and accepting unanimous constraints of pooled procurement. Therefore, regional procurement initiatives based on similar objectives of participant countries are more likely expected than pooled procurement for the entire European Union. Second, pooled procurement should not be considered for all pharmaceutical technologies, but only in justifiable cases, such as urgency in patient access in pandemics, low volume for patients with (ultra-)rare diseases, or social contracts on equitable access for the EU investment from public-private partnership [10]. Third, if participant countries have different economic status, differential pricing should

be considered to facilitate equity in health care financing across countries. Fourth, the efficiency of pilot pooled procurement initiatives should be evaluated to clarify the appropriate scope of health technologies for future initiatives and to provide recommendations for the most important barriers.

2.4. Area for harmonized action #4: ad-hoc procurement of technologies with high unmet need without cost-effectiveness evidence or with high budget uncertainty

Alternative access schemes (AASs) outside the standard positive drug list for high-cost and potentially non-cost-effective technologies have become a routinely used approach in several EU countries to ensure at least partial access to patients [31]. Examples of such AASs include access programs on a named patient basis, special medicine funds (e.g. innovation funds) and national programs (e.g. the initial version of Cancer Drugs Fund in England or the AIFA 5% National Fund), financing high-cost medications through the hospital system outside reimbursement packages, coverage only in research, and compassionate off-label use for patients without alternative therapies.

AASs are the second-best solution for patient access compared with general payment models (such as positive drug listing) for several reasons. First, evidence requirements and evaluation criteria for such schemes are often unclear. As a consequence, subjective elements may play a more important role in resource allocation decisions for individual or subgroups of patients. Second, when reimbursement decisions are made on a named patient basis (i.e. individually for each patient), the process can become bureaucratic and time consuming, which may cause problems in diseases where delayed therapy initiation irreversibly worsens health outcomes [32]. Third, when AASs are increasingly used over time, it is an indicator of patient access barriers related to general payment models, or which necessitates the reconsideration of the general payment models [33]. Alternatively, the increased use of AASs can be an indicator of overutilization of cost-ineffective technologies, which provide health benefits at an unacceptable opportunity cost. Finally, AASs are not predictable for the health industry, which creates problems with preparing market access strategy or, in the worst case, creates opportunities for companies with poorer ethical standards.

Overall, there is a need for clarity on the classification of AASs, the transparency of decision criteria, processes, and stopping rules, which need to be addressed at the European level.

2.5. Area for harmonized action #5: lack of affordability for potentially curative technologies with high upfront cost

Health care payers have mostly been managing affordability constraints of new medicines by price capping or volume control arrangements [34]. Affordability is a huge concern for health care payers and the society in case of potentially curative, but individually manufactured cell and gene therapies with high initial costs. These therapies have the potential to offset future health care and societal costs through these initial investments [35]; however, at the time that the value-based price must be determined and an initial decision needs to be made on the financing of these medicines, there is often not yet a guarantee for long-term benefits for either the entire patient population or for individual patients. A prospective approach to evidence generation and payment needs to be implemented [36]. Uncertainty in long term clinical outcomes naturally corresponds with considerations of delayed payment. However, implementation of delayed payment is hardly feasible in the current legal context and financial planning practice in many jurisdictions [37].

The scientific literature describes delayed payment models, annuity/leasing payments or payments after positive outcomes instead of the upfront payment for medicines, or payment at use for reimbursed medicines as potential solutions. These models have been experimented with in early technology adopter countries; however, several barriers prevent their implementation on a larger scale and across European countries [38], which may affect the access of patients to promising technologies with high upfront costs. Recent studies have shown that there is still a large discrepancy between experiences and perceived attitudes regarding payment models in different settings [25]. This necessitates a coordinated action across multiple stakeholders within and across countries [38,39].

3. Conclusion

In the European Union, pricing and reimbursement of health technologies is a competence of member states, which cannot be challenged [40]. While policymakers in different countries can potentially make important steps to redesign pricing and reimbursement models for new technologies as a response to the abovementioned challenges in their own jurisdictions, if policy changes go into different directions in EU member states, heterogeneity of evidence requirements and complexity of payment models in the current EU policy environment with negative externalities (due to external price referencing and parallel trade) can worsen the competitiveness of European pharmaceutical R&D.

On the other hand, if recommendations are developed in a European context with the involvement of multi-stakeholder groups, including regulatory agencies, HTA bodies, health care payers, patient organizations, and with input from the pharmaceutical industry, there is a higher likelihood that such payment models can secure affordable and equitable patient access to high cost and/or high budgetary impact medicines. Due to the standardization process, health technology developers can make more appropriate judgment on the common denominator for evidence requirements by key policy-makers, including regulators, HTA bodies, and health care payers in different countries. By relying on a streamlined evaluation process, pharmaceutical companies may cut the time to market access and pay attention to openings in new markets, which may contribute to faster access to innovative health technologies by patients and health care providers.

Ultimately, through these achievements, there is a potential to make progress in several scientific, societal, and economic objectives. The European Union HTA regulation provides a framework for collaboration on horizon scanning, evidence generation (through joint scientific consultation per- and post-approval), and joint clinical assessments. Although the harmonized use of previously piloted payment models is not within the scope of the EU HTA regulation, the regulation may be a facilitator for the exchange of ideas and collaboration within the EU on the topics discussed in this paper.

4. Expert opinion

Policymakers in different European countries face an important trade-off, whether they should opt for improved and more equitable patient access to more new medicines across EU member states by giving up a part of their national (or personal) preferences for implementing special value judgment methods and unique payment models, or that they remain purely nationally focused and ignore the reality of multinational pharmaceutical companies and their call for more clarity on the common denominator for health economics and outcomes research evidence requirements and payment models in the European Union.

Policymakers and health care payers may not have a different opinion from pharmaceutical companies, health care professionals, or patients on the ultimate objective of pharmaceutical R&D. Societies should find efficient ways to facilitate public and private R&D in parallel with creating equitable and sustainable patient access to new medicines. Different stakeholders believe that the extension of current value frameworks with additional value elements and development of novel payment models can facilitate patient access to new high-cost medicines, which may be a fair assumption in the short run. However, if evidence requirements and market access pathways become increasingly complex and different in each country, the expectations of health care payers in the majority of countries cannot be satisfied by global pharmaceutical companies, which may ultimately reduce equitable and sustainable patient access to innovative technologies and negatively influence return on pharmaceutical R&D investment. At this point, it will become clear to most stakeholders what the authors believe today: the highest need is not the design of additional novel payment models, but the uptake and more aligned use of previously piloted payment models in EU member states.

Such a movement cannot happen without a pan-European initiative and commitment of multiple stakeholders to three underlying principles: solidarity, transparency, and sustainability [41]. However, as pricing and reimbursement decisions need to be made at national level in EU member states, the success of a pan-European initiative for alignment of payment models to i) improve patient access to innovative pharmaceutical technologies, ii) to improve the sustainability of healthcare financing and iii) to facilitate pharmaceutical R&D in the European Union, will depend on country-specific adaption to local needs and requirements.

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