

14. Market Access Hurdles in Developed Countries

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14.1 Introduction

In most countries, the current and future healthcare challenges are set against concerns over healthcare budget growth, due to the aging population, an increased incidence of chronic diseases, and an easier access to a large repository of health information. On the other side, the rapid pace of therapeutic innovation (advanced therapies, personalized medicines, gene therapies, tissue engineering) and the rising costs of innovation in healthcare (the ever-growing complexity and cost of clinical trials, companion diagnostics, genomic profiling, the requirements for post-launch observational studies) make the prices of medicinal products inevitably higher. Rising healthcare costs represent an unsustainable trajectory for payers in the developed markets, which created additional hurdles for Pharma companies in ensuring access to new medicines. Until a few decades ago, only safety and efficacy guided the decisions about the reimbursement of medicines,

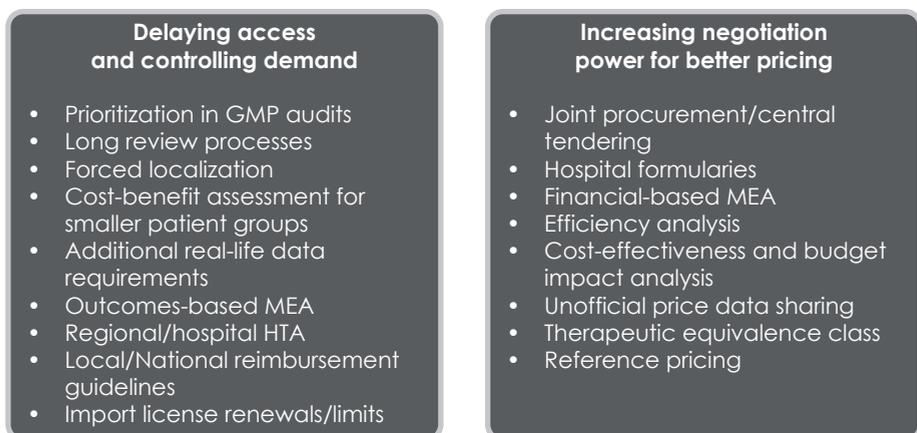


Figure 1. Categorization of Market Access Hurdles

GMP = Good Manufacturing Practice; MEA = Managed Entry Agreement

whereas today decisions are made based on cost-containment rationales. As a result of these challenges, market access hurdles for medicinal products have become more diversified in the last two decades, and they can be categorized into two major types (Figure 1), based on the payers’ needs and capabilities:

1. Delaying access (long review processes, real-life data requirements, cost-benefit assessment for smaller patient groups, prioritization in Good Manufacturing Practice audits before registration submissions, unscheduled Review Committee Meetings, regional/hospital reviews, outcome-based managed entry agreements) and controlling demand (local reimbursement guidelines, import license renewals/limits, forced localization).
2. Increasing negotiation power for better pricing (cost-effectiveness and budget impact analysis, joint procurement, central tendering, separate budgeting, hospital formularies, efficiency analysis, therapeutic equivalence class, joint Health Technology Assessment initiatives, unofficial price data sharing, reference pricing, financially based managed entry agreements).

Delaying Access and Controlling Demand

Before the 1990s, efficacy, safety, and quality were the key parameters when deciding the reimbursement of new therapies. Once a drug was registered in a country, it was automatically reimbursed and became available to patients, as per its label. Hospital formulary listing was the only barrier for budget holders considering the price of the new drug, which was influenced by prescribing physicians convinced of its clinical benefit. Starting

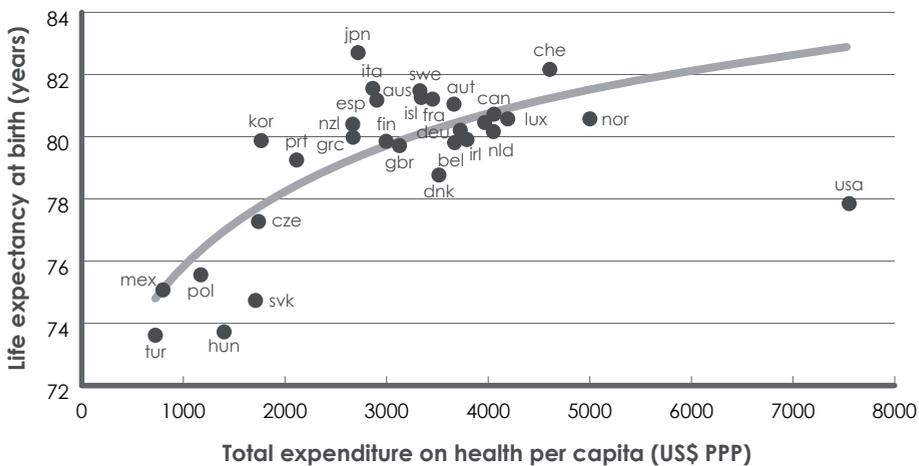


Figure 2. Differences in life expectancy and healthcare spending across OECD countries. Modified from [OECD 2010]

from the 1990s, efficiency became more important: with the increase in healthcare expenditure, the improvement of effectiveness in the use of limited resources, in order to find the best way to support a high quality of care, gained more importance for policy-makers. Multiple perspectives were developed to avoid any overuse/misuse, and waste of resources, and the three new data requirements for the evaluation of new products became cost-effectiveness, budget impact, and quality of life. Since 2010, value has become the key factor, so value-based healthcare has become an emerging new paradigm to control costs while ensuring the quality of care. It is fundamental to boost innovation on the part of the suppliers, in order to create value for patients and improve their outcomes.

The concept of value obtained by reducing inefficiencies without compromising the access to quality has emerged as a patient-centric approach, and gained even more importance. Achieving value for money in the healthcare sector is an important objective in developed countries. OECD estimated that the average life expectancy could increase by about two years for the OECD as a whole, if resources were used more efficiently. It was reported that countries that spend the most are not necessarily the ones that fare best in terms of healthcare outcomes. Policy reforms able to increase value for money, in order to increase efficiency, have become one of the top priorities.

One of the most common mechanisms used by payers is to delay access to the market for new and expensive treatments and reduce the volume by trying to control their consumptions. Because of these efforts, a paradigm change occurred, evolving from the traditional payment model based on fee-for-service to value-based healthcare. The traditional system provides incentives for the volume of service performed: this gave rise to concerns about increasing costs and poor performance on quality indicators. Therefore, hospital administrators, private insurance schemes, and public care providers started a transition towards value-based payment models in order to improve healthcare outcomes. New funding and distribution mechanisms for high-cost medicines (i.e., managed entry agreements) have become a tool to provide certainty about the performance of a new treatment for clinical outcomes and the patient health status, including physiologic and mortality measures. Many Pharma companies and medical device manufacturers started using these innovative agreements, which vary across many forms of deal, including shared risk, bundled payments, and volume capitation, in order to overcome the access challenges.

With the introduction of the new funding mechanisms, developing evidence and demonstrating outcomes in real-world studies gained increasingly more importance, because of the possibility to show both the clinical and economic superiority of the new technology vs. the existing alternatives. Furthermore, hospital-level HTA has emerged to improve productivity gains by focusing on the efforts to understand, quantify and improve the efficiency and value in the delivery of healthcare services, taking into account not only drugs and devices but also personal time, supplies and interventions. Many quality and efficiency measures have been introduced in hospitals, ranging from internal quality improvement measures, pay-for-performance incentive schemes, and physician treatment guidelines, including reimbursement guidelines, especially for new technologies. While these tools and measures have increased value gained from technol-

ogies, the time needed for assessment has delayed access to innovation. In order to reduce market access delays, drug manufacturers should work on data generation, setting value-based criteria for reimbursement, conducting health economics models with payers at different levels.

Increasing Negotiation Power for Better Pricing

Despite the efforts implemented by the European Commission to expedite the pricing and reimbursement procedures among European Union member countries, the opposition from national governments and members of the European Parliament steadily increased the average delays and time gaps among the countries. In 2002, the EU Commission and the Health Council (consisting of the Health Ministers from the EU Member States) actively supported cross-border collaboration in health technology assessment, which could partly accelerate market access and decrease the gaps between the countries. Finally, in 2004, the European Commission and the Council of Ministers positioned Health Technology Assessment (HTA) as a political priority and urged the establishment of a sustainable European network on HTA. In 2005, 35 organizations throughout Europe answered the European Commission's call and the EUnetHTA Project initial activities started. EUnetHTA Project aims to support the collaboration between European HTA organizations and bring added value to healthcare systems at European, national and regional level. Throughout its activities, this project developed alliances and cooperation among HTA organizations. A report adopted by European Parliament in March 2017 once again highlighted the delays between Marketing Authorization and the subsequent decisions on pricing and reimbursement, the unavailability of products due to budget constraints and the high prices of new technologies and the inequalities of access among countries and regions.

Although there are strategic actions for improving the quality and timing of the technologic review process, pricing and affordability remain the most important reasons behind the real barriers to access. Alternative pricing methods were developed to overcome the payers' concerns at product launch and issues with the international reference pricing. Besides, EU explicitly stated the need for the new approaches to control the increasing financial pressure of new high-priced medicines, to improve patients' access to medicines and to promote innovation. The report "Study on enhanced cross-country coordination in the area of pharmaceutical product pricing", published by the European Commission in December 2015, focused on the international reference pricing, and proposed solutions based on sharing net prices, EU coordination mechanism and mechanism for differential prices. Experts recognized the difficulties in implementing the proposed mechanism (such as political will, legal constraints, agreements between the Member States) and the ineffectiveness of these measures in improving the access to medicines. Again, they came up with the proposal of implementing new pricing policies, such as joint procurement initiatives, which were not within the scope of the EU report. Joint procurement proposals were also mentioned by other international organizations and by politicians: in January 2016, OECD claimed pharmaceutical compa-

nies have excessive power in price negotiations, and recommended new approaches to fight the upward trend of launch prices. In March 2016, at the G7 meeting, France proposed other price-control solutions for innovative medicines, and other European ministers explicitly supported the idea by forming new collaborations and bilateral agreements (Benelux and Austria collaboration, Central and Eastern European collaboration, Mediterranean Countries collaboration, Nordic collaboration, Portugal and Spain bilateral agreement for sharing experience and data). Joint procurement discussions, aimed at strengthening the purchasing power of payers, spread out quickly in other regions of the world (Latin America, Eurasia). The Joint procurement related price control mechanism increased the concerns of the life science companies about the payers' deliberate efforts to decelerate the access to new expensive medicines by creating another hurdle, along with the national and regional ones.

14.2 Regional Access Hurdles

In the last decade, with the political empowerment of the regions and the trends for shifting central fiscal discipline to the regions (10 provinces in Canada, 6 states in Australia, 16 lander in Germany, 21 regions in Italy, 17 regions in Spain, 12 regions in Netherland, 21 counties in Sweden) for a more effective control of the health spending, regionalization in healthcare funding became more prominent even in highly centralized countries. However, initial price negotiations remained in the hand of the national authorities, and additional price and volume control mechanism are used by regional payers according to their capabilities and purchasing powers. The growth of regional payers may not be only a simple replication of the national decisions, and regional payers may use different methods to evaluate health technologies, by focusing on other components of market access (i.e., cost-effectiveness for nationwide decision vs. budget impact in the regions. The variety of the decisional analysis tools used by regional payers and their negotiating power require companies to develop different pricing and reimbursement approaches and data types. While payers at national level can decide on issues such as initial Marketing Authorization, prices and reimbursed population, payers at regional level can effect entry date, local marketing activities, restrictions to prescriptions, local recommendations for physicians, physician-company interactions for promotional activities, creation of therapeutic areas. Decision-makers, influencers, and content of data requirements also vary among regions, making market access processes more complex. From the patient's perspective, there is a growing risk of access inequalities due to different efforts by central governments to control regional budgets.

Hospital-Based HTA

Hospital-based HTA is a relatively new concept, which was developed after a nationwide discussion on the impact on end users of large-scale HTAs. It basically consists of

the implementation of processes and methods of HTA at hospital level. Although it's generally performed with the resources of the hospitals, it can also be outsourced to independent HTA bodies. It is developed to answer the questions by hospital managers or budget holders relating to the implementation of new technologies and the efficient use of existing technologies in their hospitals. The main objective of the hospitals is the critical appraisal of health technologies on effectiveness, tolerability and reducing overall costs and

Pros	Cons
<ul style="list-style-type: none"> • List prices to remain at launch price and minimized risks of international reference pricing. • Risks on the payer's side are minimized by reducing the element of uncertainty of product performance. • Generate evidence in the real-world setting. • Gain market access without compromising on the launch price of the drug. • Pay-for-performance schemes foster price negotiations by reinforcing value messages. • Conditional reimbursement based on registry enrolment reduces inappropriate/off-label use. • Price-volume agreements provide more stable pricing and reimbursement environment and offer payers a budget impact predictability. • Price-volume agreements can be used as a cost containment tools, together with prescribing control mechanisms. • Performance schemes associated with patient responses may influence the earlier uptake by physicians. • Patient-based caps encourage the adherence to label, to produce maximum response. • Investments in innovation are boosted. • Payers have the flexibility to limit the impact of the introduction of new drugs, together with horizon scanning activities and price revisions based on post-marketing surveillance. 	<ul style="list-style-type: none"> • Additional resources and investment needed to monitor patients or to comply with the agreement conditions by manufacturer, provider, and payer. • Additional costs are incurred in managing the schemes. • Manufacturer may be responsible for the loss of non-responding patients. • Payers may propose to use data management systems set to monitor patients' clinical progress as cost management tool. • Negotiations with payers start at a higher price level at launch, if manufacturers foresee the risk of price cuts based on the outcomes. • Price-volume agreements may not ensure an on-label or appropriate use. • Schemes do not remove all financial uncertainties of use (high demand, resulting in greater-than-anticipated long-term costs). • Schemes may restrict patient access to products, due to the administrative hurdles in real-life. • Not all schemes are useful for patient access (e.g. limited access if budget cap is reached). • Difficulty to set stopping rules for agreement or for the withdrawal of the product when unsuccessful. • Duplicated and fragmented data collection efforts for multiple countries.

Table 1. Summary of the pros & cons of performance/outcomes-based managed entry agreements

ensuring the rational use of their resources. Joint decisions made by hospital groups also involve a decrease in the geographical variation in the availability and access to health technologies. There are many reasons for the emergence of hospital-based HTA: global/national recommendations of existing HTA agencies may not answer precise local questions, long assessment periods for national decisions delay the access to expensive new technologies at large research hospitals, all technologies are not evaluated at national level, but they can be medically or economically critical at hospital level. Unfortunately, the lack of transferability of the results in hospital-based HTA causes the duplication of work, with several medical institutions evaluating the same technology. Despite the increasing use of hospital-based HTA, there is limited know-how about its practice and impact. HTA at this level can also be considered as a threat to restrict the clinicians' independence in decision-making. Because of the slow assessment process, when considering critical health results of new technologies, clinicians are not willing to wait for months for a decision. A more frequent use of hospital-based HTA and its wider implementation could help national HTA agencies benefit from their work and observe the results of nationwide decisions at patient level. It should be supported by a political and managerial willingness to smooth out implementation issues and by a reformist approach to the local decision-making processes. Nevertheless, hospital-based HTA practices are progressively increasing, therefore experts in the area already noticed the need for guiding principles and organizational models .

Managed Entry Agreements

Managed Entry Agreements (MEAs) are accepted, at least in theory, as an enabler for pharmaceutical companies to gain earlier market access, and as an opportunity for a fast access to innovation by patients. However, in practice, this process can be transformed into a never-ending vicious cycle of negotiation. There are comparable pros and cons for the implementation of MEAs (Table 1). Due to these risks and difficulties, the industry and the payers have become more and more reluctant to use them.

In most countries, MEAs have been implemented upon the manufacturers' request to facilitate the negotiation process. For instance, in Italy there is no specific law regulating the process; rather, it is decided on a case-by-case basis. However, the Italian Medicines Agency (AIFA) implemented different types of MEAs for each newly launched medicine that presents some uncertainty with regard to clinical effectiveness, budget impact, or potentially inappropriate use. In the UK, MEA proposals are the responsibility of the pharmaceutical companies. Companies can propose MEAs either at the time of the initial submission for assessment, or at the end of the evaluation process. There are no well-defined timelines for implementation, and the average duration of the process varies among the countries and depending on the type of MEA. A lengthy process can create a bottleneck for a timely access to innovative medicines. In any case, it has gained more importance, and there has been a steady growth in the number of agreements implemented.

14.3 The Next Challenges

The rapid pace of therapeutic innovation and advanced technologies might substantially extend the survival times, and even cure severe chronic diseases. However, delayed access and price pressures are expected to continue as long as the payers' concerns on budget pressure persist. While drug companies are trying to meet the decision-makers' expectation on the demonstration of the value of innovation, they are exploring new ways of doing business with the spread of digitalization and the empowerment of patients to make informed healthcare decisions. Patient-centric approaches are becoming more and more common, to increase the demand for healthcare services despite the demand control mechanism induced by payers. Digital solutions are becoming critical to meet the needs of patients, to ensure adherence to treatment, and to show outcomes that meet the payers' expectation. Thus, Pharma companies are increasing the use of digital technologies to obtain real-world efficacy data.

With the recent evolution of the business model, the importance of the patients' decision in the choice of their treatment is increasing. It also enables payers to implement risk-sharing schemes based on adherence, daily measured criteria, and quality of life. Policy-makers should establish an infrastructure for the management and digitalization of information, and encourage value-based competition, by reducing new entry barriers. Rapid assessments and common databases can also be used to decrease the discrepancy between HTAs carried out by different bodies, to ensure a timely access to medicines on the part of patients.

14.4 In summary

- Price pressure will continue to affect budget holders and the business, economic and scientific methods used to increase decision-making efficiency.
- The decision levels will increase and access will be inevitably delayed.
- Equity in access will remain problematic, because of reimbursement filters by different local and regional payers, and across countries.
- The lack of coordination among layers/regions/countries is obvious, but efforts will continue towards harmonization.
- Financial risk will shift more towards Pharma companies, increasing access hurdles.
- Hurdles start before registration in many low affordability markets with other methods of supply restrictions (GMP, import quotas, forced localization).
- After launch, there are continuous barriers: price reviews, reimbursement restrictions, delisting.
- Digitalization will continue to emerge daily, to increase health literacy and the generation of patient-driven demand for informed decision-making.

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