MEDEV
Medicine Evaluation Committee

Reflection on national strategies for new medicines coming to the market

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1. List of Abbreviations

Abbreviation	Definition
ATMPs	Advanced Therapeutic Medicinal Products
Beneluxa	Cooperation of Belgium, Netherlands, Luxemburg, Austria and Ireland
CMA	Conditional marketing authorisation
EU	European Union
EEA	European Economic Area
EMA	European Medicines Agency
EUnetHTA	European Network for Health Technology Assessment
FINOSE	Cooperation of Finland, Norway and Sweden
HTA	Health Technology Assessment
IPR	Intellectual Property Rights
MA	Marketing Authorisation
MAH	Marketing Authorisation Holder
MEA	Managed Entry Agreement
MEDEV	Medicine Evaluation Committee
MoCA	Mechanism of Coordinated Access to Orphan Medicinal Products
OECD	Organisation for Economic Co-operation and Development
P&R	Pricing and Reimbursement
RCT	Randomised Controlled Trials
R&D	Research and Development
TRIPS	Trade-Related Aspects of Intellectual Property Rights
Visegrad group (V4)	Cooperation of Poland, Czech Republic, Hungary and Slovakia
WHO	World Health Organisation
WTO	World Trade Organisation

2. Executive summary

Decisions on pricing and reimbursement of new medicinal products are a national competence. Thus, each EU Member State negotiates individually with a limited number of largely globalised manufacturers for globally marketed products. The accelerated pace of technological developments, increasingly complex therapies and the combination of different technologies is changing regulatory practice, influencing HTA as well as pricing and reimbursement practices.

Innovative medicines targeting a (high) unmet-medical-need often demand marketing authorisation through an expedited procedure based on much less robust evidence than in the past, leading to higher uncertainty of effectiveness and safety. Extremely high prices endanger affordability for patients and the sustainability of health systems. In this changing environment, payers must still continue to ensure that decisions on access to safe and effective therapies are based on sufficient evidence and that prices reflect the actual added benefit to patients (and/or health systems). Thus, new products receiving marketing authorisation by way of expedited procedures present a challenge to current practices.

Stakeholders are insufficiently aware of the differences between a regulatory decision, based on the expected benefits outweighing the risks, and the quantification of proven benefits as a basis for payer's decisions on pricing and reimbursement. Therefore, for new products receiving market authorisation by way of expedited procedures, mechanisms have to be implemented to deal with uncertainties and to reduce the risk of spending public money on ineffective or unsafe therapies.

Payer organisations are already considering or implementing changes to deal with these challenges. These changes include:

- conducting horizon scanning to identify products early in their development that might need additional action (pre- and post-launch);
- entering into early discussions with the regulator, HTA, patient representatives, health care professionals and market authorisation holders (MAHs) to influence the evidence that is generated pre- and post-market launch to reduce uncertainties;
- issuing conditional reimbursement decisions, or refusing reimbursement for the public system;
- deriving pricing decisions dependent on the level of available evidence of added patient benefit, with the flexibility to adjust the price based on new evidence generated (e.g. through Managed Entry Agreements (MEAs)),
- exploring options for developing a pricing model for deriving a fair price, as a basis for negotiations with (MAHs);
- developing criteria for the use of new products (appropriate use), including requirements for health professionals and institutions;
- providing appropriate information to patients and health professionals;
- monitoring the use of the new product by collecting/analysing routine data or using special tools;
- assessing the budget impact based on estimated numbers of patients that can benefit from the new therapy;
- initiating collaboration between payer institutions at regional/national and European level;
- concluding financial agreements on volumes and associated prices.

This paper is a reflection of how the above-mentioned issues are extending the current role of payers. The changing environment demands closer cooperation of payers with regulators, HTA, health professionals, patient organisations and MAHs.

3. Introduction

This reflection paper is based on discussions in the "payer community" and is meant to support a structured approach to providing access to new medicinal products entering the market. It also provides an insight to other stakeholders on how the payer community is addressing the current challenges and thus paves the way for intensified cooperation.

In the context of this reflection paper, access for patients means the (partial) reimbursement of medicinal products by public health systems. Private access is possible after marketing authorisation (MA) is granted by the regulator, but for most patients, new therapies are not affordable on a private basis.

The dynamic developments in the pharmaceutical market require complementary actions by payers in order to maintain the sustainability of their health systems and at the same time provide access to new medicines, especially those addressing a high unmet medical need. These developments require action at national level but also at European level. European action is beneficial as the supply market for medicinal products is global and all Member States' health systems are confronted with the same new products and have to negotiate with the same MAHs. Member States started to assess new medicines together in the various EUnetHTA Joint Actions and an EU regulation is under discussion to establish a permanent EU cooperation on the assessment of medicines and medical devices at the EU level.

The payer's decision-making process on access and prices is based on the assessments of the regulator, HTA institutions and the payers themselves. Early cooperation between all stakeholders will be key to managing uncertainty, as it allows for appropriate consideration of their respective data requirements. In addition, a common understanding between regulator, HTA and payer organisations of what constitutes unmet medical need, could lead to shared decisions on the appropriateness of expedited pathways and conditional approvals. Patients' access will also depend on manufacturers that respect their social responsibility in this very special market and are willing to negotiate fair prices to ensure the sustainability of public health systems. A lack of progress in this field is driving payers to call on national and EU political institutions to ensure fair pricing as discussed in the WHO[1].

The COVID-19 pandemic underlines the need for cooperation amongst all stakeholders, as new vaccines and therapies are being developed and must be made accessible to all patients.

[1] https://www.who.int/medicines/access/fair_pricing/en/

4. Role of payer organisations

The Medicine Evaluation Committee (MEDEV) is a platform of public, not-for-profit, "payers" in the health sector of the EU/EEA, which are responsible for access to and financing of medicines for the populations they serve.

Public payer organisations are a very heterogeneous group of institutions and encompass governmental organisations and social health insurance organisations financed from taxes and/or obligatory health insurance contributions. In some Member States, the payer and HTA (and even regulator) functions are combined in one organisation. There is no explicit common statement on the vision and mission of payer organisations but the main elements can be summarised as followed:

Payers' Vision: The population we care for has access to high-quality affordable health care services and we support the population in maintaining their own state of health to the highest possible level.

Payers' Mission: Payers strive to provide patient-access to high-quality care, allocating public financial resources in an optimal way. Best possible care translates into improved health for the population we serve. Care should be safe, effective, efficient, timely, affordable and equitable.

5. Technological and regulatory developments

In the past, the development of new medicinal products and innovations was largely driven by blockbuster strategies, targeting high prevalent diseases such as diabetes or cardio-vascular diseases. Over the last decades, biological medicines have gained importance in an increasing range of indications and have started targeting rare diseases (encouraged by the EU orphan legislation) and in the last few years, gene and cell-based therapies (Advanced Therapeutic Medicinal Products, ATMPs) have entered the market. These new therapies have the potential to make a substantial positive impact on the health status of patients, extend survival and improve quality of life. Certain therapies might even potentially cure diseases that are currently chronic or fatal. ATMPs (gene therapy, somatic cell therapy and tissue engineering products) are expected to account for up to 25 % of new MAs in the coming years[2]. The assessment of these products is complicated by small study sample sizes, the use of surrogate endpoints and short-term follow-up. For some new products, eligible patients have to be identified prior to treatment initiation by using, often expensive, diagnostic tools (biomarkers, DNA tests, etc.) that also need to be validated. Moreover, combinations of medical devices and medicinal products pose new challenges for assessing the added benefit.

These new therapies can address a high unmet medical need. Core elements of unmet need are the lack of alternative treatment options, disease severity and incidence/prevalence of a disease (orphan designation)[3]. If there is a high unmet medical need, all stakeholders are committed to make new, effective and safe therapies that address this need available to patients.

New effective treatment options or even cures (with one "shot") for rare diseases are good news for patients, but the pricing of these products is increasingly endangering the

[2] EMA, Hans-Georg Eichler, Senior Medical Officer, Presentation Vienna 2019

[3] Wim Goetsch et al, Unmet Medical Need: an Introduction to Definitions and Stakeholder Perceptions, Value in Health, 2019, https://www.sciencedirect.com/science/article/pii/S1098301519323034

sustainability of health systems. This is aggravated by the fact that for most of these new products, proof of sustainable effectiveness has yet to be established.

Products with an orphan designation account for an increasing percentage of new market authorisations granted by EMA: from 22 % in 2011 (5 out of 23) to 46% in 2018 (17 out of 37). Nevertheless, new products for ultra-rare diseases are still the exception. In a market-driven environment, the focus remains on high return on investment and this explains why so many new products are being developed for cancers and why prices demanded for treatments for hereditary diseases are often excessive.

In Europe, most new medicinal products are granted MA by the European Medicines Agency (EMA). The European decision makers (European Commission, European Parliament, and European Council) support the EMA in their efforts to identify (high) unmet medical need and foster innovations in this field, making products - with substantial benefit for patients with a high unmet medical need - available on the European market in a timely way. EMA, along with other important regulatory agencies in the world (FDA in the USA and PMDA in Japan), has introduced expedited approvals for new medicines that tackle a major public health interest, particularly from the point of view of therapeutic innovation. These approvals are often based on a low level of evidence of safety and efficacy as the products often target small patient groups, and high evidential standards like Randomised Controlled Trials (RCTs) are not conducted. This leads to a much higher level of uncertainty at the moment of (conditional) MA. The fear that EMA is lowering evidential standards is addressed in several publications[4]. According to the European legislative framework for pharmaceuticals, EMA is committed to give MA when the benefit-risk ratio is assessed to be positive. Payers are demanding greater involvement and more transparency regarding the methodology and criteria used in these assessments, especially when decisions are based on little data. At the same time, EMA is aware that other criteria are used for national decisions on pricing and reimbursement and that patient access to medicines can only be realised through the joint efforts of all stakeholders. The EMA strategy "Regulatory Science 2025" introduces a plan to involve HTA and payer organisations early in the process and in pre- and post-launch evidence generation, to enable better and timely decision making by all institutions involved in patient access.

New products addressing a high unmet medical need can get expedited approval from regulators based on limited data: "…[For] medicinal products for human use which are of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may request an accelerated assessment procedure" [5]. Moreover, products may receive conditional marketing authorisation CMA, even if the level of evidence on safety and efficacy is low: "In the interest of public health, it may be necessary to grant MA on the basis of less complete data than is normally the case …"[6]. CMA obliges MAHs to provide the missing evidence post-launch. Expedited approval and CMA have led to an increase in MAs being granted with a preliminary positive benefit-risk-ratio appraisal based on limited data and with the need for post-launch evidence generation. These procedures risk shifting at least part of the product development costs to payers.

HTA organisations assess to what extent a new product is better than existing therapeutic alternatives (comparator). However, many studies provided in the framework of regulatory approval do not allow a comparison with other products or quantification of added benefit.

[4] Yannis Natsis, Policy Manager Universal Access and Affordable Medicines, EPHA, THE TOP 5 ISSUES IN MEDICINES POLICY FOR 2019, February 2019

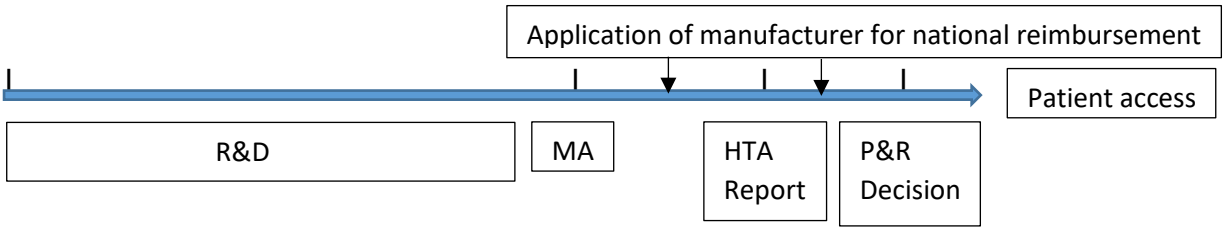
[5] Art. 14(9) 2004/726/EU

[6] EC 507/2006, 29 March 2006

The level of evidence can be so low, that there is no solid basis for advice on reimbursement and pricing. Payers nevertheless have to derive reimbursement decisions. This leads to the unsatisfactory situation where many expensive therapies are available on the market and reimbursed by public health systems without robust evidence of their safety and efficacy.

From product development to patient access

The standard process from research and development (R&D) via MA, Health Technology Assessment (HTA) and pricing and reimbursement (P&R) decisions to patient access is sequential and can be outlined as follows:

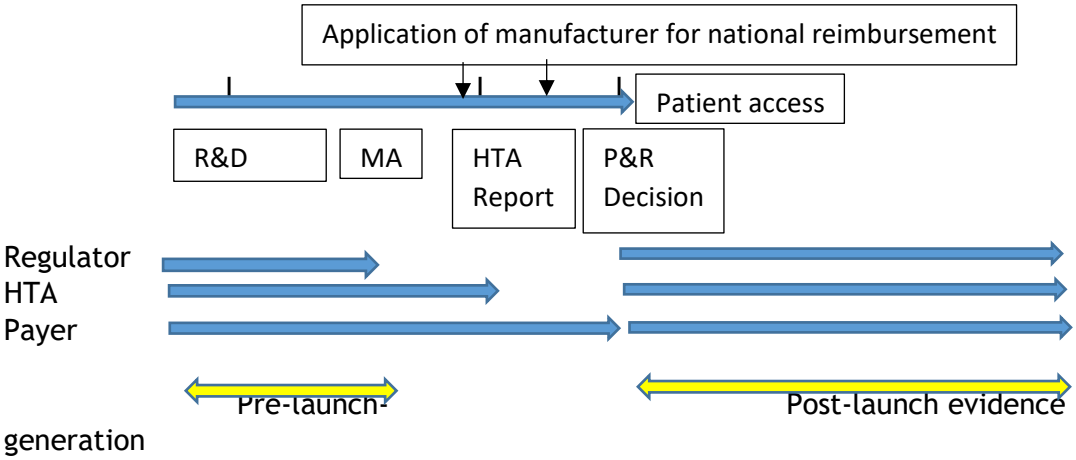


This standard procedure includes comprehensive studies (Phase III studies, where possible RCT). Once MA has been granted, pricing and reimbursement decisions have to be derived. These may be based on HTA, including the assessment of added benefit compared to other therapeutic alternatives. If applicant MAHs are willing to provide (confidential) data to HTA institutions early on, the HTA report can be issued closer to the time of MA. However, patient access also depends to a large extent on the marketing strategy of the manufacturer and thus on its willingness to introduce new products into the national systems.

When a high unmet medical need is identified and there is a reasonable expectation that the product will substantially improve relevant patient outcomes, an expedited procedure can bring a potentially successful product faster to the market and to patients. To enable expedited decisions by HTA and payer organisations on pricing and reimbursement parallel assessments by regulators, HTA and payers would be useful. Such a procedure would require the cooperation of applicants, who need to submit data and allow for information exchange between authorities in advance of regulatory authorisation.

However, expediting HTA and payer decision-making does not solve the problem of the lack of data available for many products aiming to address high unmet medical need. Insufficient data may only be acceptable if the obligation to generate more evidence before including the product in the reimbursement system would unacceptably prevent patient access to the new treatment. In the payers' view, not all products receiving CMA fulfil this condition.

In order to allow timely patient access to new medicinal products with a high unmet medical need, while simultaneously reducing uncertainties for payers, collaboration between all stakeholders is needed, with processes running as far as possible in parallel. Early collaboration between regulator, HTA and payers must therefore include a discussion on which products are eligible / accepted for expedited procedures and what level of evidence must be generated before MA. Conditional decisions will lead to post-launch evidence generation.



CMAs will result in obligations for the MAH to generate additional information and in reassessments by the regulator. The regulator must withdraw the MA if the re-appraisal of benefit-risk-ratio turns out to be negative.

Payers need to decide whether the regulatory decision to grant CMA necessitates the application of special conditions for reimbursement. If so, and if national legislation allows they may even grant conditional reimbursement and reassess at a later date if / if not to continue reimbursement in the public system. In addition, payers may decide to conclude pricing agreements with MAHs based on defined outcomes in post-launch studies. Patients and physicians must be informed about the status of the new product and know that the decision on access may change, either through withdrawal of MA or of reimbursement.

Access additionally depends on the manufacturer's willingness to enter the national market. MAHs often launch their new products in "rich" countries first, delaying access in other countries. There are several reasons why MAHs decide not to enter a market or withdraw from it:

- the market is not expected to be profitable enough; a low price in less wealthy countries might also lead to lower prices in higher income countries through price referencing mechanisms;
- the HTA assessment may lead to a maximum price decision by payers that is not acceptable to the manufacturer.

Unequitable access across Member States is criticised and political action might be needed to ensure that the MAHs, receiving central MA for a new product in the EU, have the obligation to make the product available in all Member States in a timely manner.

6. Managing clinical uncertainty regarding safety and efficacy

Payers manage public funds and are therefore obliged to base their decisions on reimbursement and pricing on the added value compared to other therapeutic alternatives (clinical assessment), budget impact and/or cost effectiveness. For many new pharmaceuticals, the added value is not known at the time of MA. Through horizon-scanning and early dialogues with applicants and regulators, payers can identify new products before they receive MA and therefore shape evidence generation to their needs early on in product development and prepare for possible actions post MA.

- Post launch evidence generation

  In the post-launch phase, payers need access to relevant clinical data. Thus, guidance needs to be developed for payers/authorities to access data in line with the General Data Protection Regulation. Moreover, there is a need for consolidation between the various on-going projects on the use of everyday clinical data (i.e. real world data) and the methodologies that may contribute to a better appraisal of effectiveness and safety after product launch.

  Post-launch evidence generation requirements tied to conditional reimbursement and pricing decisions allow payers to withdraw reimbursement completely (stop criterion) and/or to negotiate new prices. Payers may also introduce performance-based MEAs to allow early patient access while sharing the risk related to uncertainties about a product's actual performance in clinical practice. Ideally, data requirements are already well defined prior to MA making timely and comprehensive data collection the main challenge. Depending on the characteristics of the missing data, the potential for biases needs to be taken into account. In addition, comparative analyses to other alternative treatments must be possible. In the case of registries, disease-related and not only product-related data are necessary. Agreements with the registry holders must be concluded in a timely manner.

  Under these circumstances, it is important that authorities and physicians inform patients about the uncertainty associated with the new product and the preliminary reimbursement of the therapy. Patients must be aware that if the final assessment of the added benefit of the therapy is negative then he or she may have to change their treatment.
  Even though performance-based MEAs can be concluded with the manufacturer to mitigate financial uncertainties, these arrangements have not yet proven to be a viable option according to an OECD study[7], mainly due to the lack of relevant data and lack of transparency. However further pilots and studies are ongoing. In addition, it has been shown that MAHs respond to MEAs by increasing list prices[8].

- Restricting the use of new pharmaceuticals

  For new products that have received CMA based on insufficient evidence of efficacy and safety, treatment might be restricted to defined patient groups and /or specialist health care facilities. Restricted use should prevent inappropriate use and optimise

[7] Wenzl, M. and S. Chapman (2019), "Performance-based managed entry agreements for new medicines in OECD countries and EU member states: How they work and possible improvements going forward", OECD Health Working Papers, No. 115, OECD Publishing, Paris, https://doi.org/10.1787/6e5e4c0f-en.
[8] Gamba et al.: The impact of managed entry agreements on pharmaceutical prices; Health Economics. 2020;1–16, DOI: 10.1002/hec.4112

high quality data collection. Prior approval by the payer organisation can ensure that pre-defined criteria are met.

- Participating in early dialogues

  Payer involvement in early dialogues can help to ensure that pre and post-launch clinical trials and studies are designed to generate the data relevant to payers' decision making.

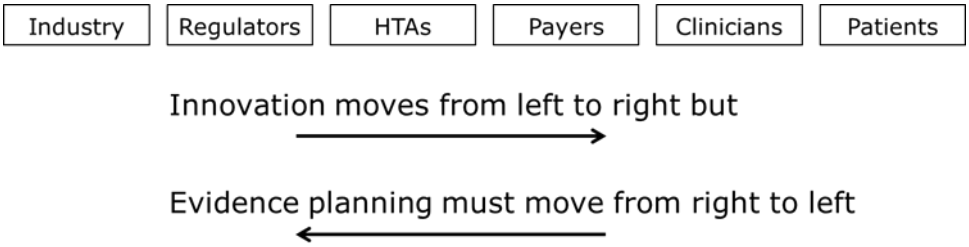
  MEDEV has several years' experience in early dialogues for new products for rare diseases (Mechanism of Coordinated Access to Orphan Medicinal Products - MoCA) and plans to pilot a process of post-launch evidence generation planning with EMA, EUnetHTA, patient organisations and MAHs. This new role of payer organisations will require the engagement of qualified staff to ensure the success of the process.

- Appropriate care

  In addition to restricting the use of new products under CMA, it is important to control the appropriateness of use. More and more new therapies are targeting (sub-)populations of the same disease. Complete information on the targeted patient (sub-)population, the benefits and risks, as well as the place of a new product in the treatment pathway (first, second or third line) is essential for physicians, patients and payers alike. Payers can put mechanisms in place to ensure the appropriateness of use of new, expensive therapies, to trigger start and stop decisions.

- Include patients from the very beginning

  Evidence generation plans need to include patients from the beginning in order to capture patient relevant outcomes. Several steps are needed before a product reaches patients. The process of market entry for innovative products, from early research to patient access, begins in academic centres or is initiated by industry. Evidence generation however needs to start with the patient and the identification of patient relevant outcomes. These outcomes should be reflected in the study design right from the beginning.



Source: EMA[9]

[9] EMA, Hans-Georg Eichler, Senior Medical Officer, Vienna, 2019

7. Managing financial uncertainty - pricing and budget Impact

The number of new pharmaceuticals entering the market, as well their prices, are increasingly bringing health budgets to their limits, threatening the sustainability of health systems, affordability and access. This used to be a problem of less wealthy countries but has become a problem for wealthier countries too.

Medicinal products are not “normal” consumer goods. Several market failures are inherent to health-related products, such as: imbalance of information, price-insensitive demand, complex supply and demand structures and monopolies or oligopolies. Medicinal products are developed in the private sector and manufacturers can set priorities in research and development (R&D) as well as decide on which markets the product should be made available. In price negotiations, intellectual property rights (IPR), supplementary protections certificates and other mechanisms place MAHs in a very powerful position. During the Dutch Council presidency in 2016, the question was raised as to how far this pharmaceutical model is future proof.

During the HIV health crisis, the World Trade Organisation (WTO) decided in Doha in 2001 that all patients should have access to medicines and that ambiguities between the need for governments to apply the principles of public health and the terms of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) needed to be clarified. In particular, concerns had been growing that patent rules might restrict access to affordable medicines for populations in developing countries. Many of these countries are struggling to control diseases of public health importance, including HIV, tuberculosis and malaria. The Doha Declaration specifically recognises concerns about TRIPS’ effects on prices. The Declaration affirms that "the TRIPS Agreement does not and should not prevent members from taking measures to protect public health". In this regard, the Declaration enshrines the principles that WHO has publicly advocated and promoted over the years, namely the re-affirmation of the right of WTO Members to make full use of the safeguard provisions of the TRIPS Agreement in order to protect public health and enhance access to medicines. The Doha Declaration refers to several aspects of TRIPS, including: the right to grant compulsory licenses and the freedom to determine the grounds upon which licences are granted; the right to determine what constitutes a national emergency and circumstances of extreme urgency; and the freedom to establish the regime of exhaustion of intellectual property rights (IPR). The TRIPS Agreement allows the use of compulsory licences. Compulsory licensing enables a competent government authority to license the use of a patented invention to a third party or government agency without the consent of the patent-holder. The implementation of TRIPS led to a sharp fall in prices of HIV treatments, but this mechanism has so far only been used in exceptional cases.

Another criticism is that MAHs justify their price setting policies on high R&D costs but without transparency on the actual costs. Furthermore, the contribution of public funds or tax reductions to the financing of R&D is usually considered confidential by manufacturers and not made public. Amid the COVID-19 crisis the EU is planning to provide €400 million in research grants to develop treatments and vaccines, nevertheless there are so far no clear obligations concerning the availability and affordability of the products developed under this project.

In recent years, the “pricing paradigm” of MAHs has shifted from a “cost-plus” model to a special form of “value-based pricing” model. “Cost-plus” means that MAHs based their price on the total costs of the product (R&D, manufacturing, marketing, etc.) and added a profit margin. The new industry policy embraces the “value-based-pricing” concept. This concept

is explained e.g. by the OECD[10] and can encompass HTA and other value assessments and can also be part of the pricing strategies of payers. MAHs have adopted this concept because it allows for value propositions that are not based on concrete evidence and can encompass benefits to society that are not directly related to the health sector (e.g. productivity of the workforce). The concept of value-based pricing applied by MAHs has led to increasing prices and rising profit margins. If such profit margins are compatible with financing by publicly funded health care systems is questionable. A simple chemical compound can be marketed at an extremely high price because it has the potential to avoid an expensive surgical intervention e.g. a liver transplantation. Alternatively, the price of a new gene therapy can be based on the potential savings in avoiding other costly therapies that themselves might already have been assessed as not cost-effective. In this way, MAHs can be seen to be testing society's willingness and ability to pay, especially if there is no alternative treatment available. If the "value" is estimated to be high, the actual R&D costs of the new product or the significance of the trial data plays, if at all, only a minor role in manufacturers' pricing decisions. In a monopoly situation (due to IPR / market protection), the negotiating position of payers is weak since the only alternative to paying the demanded price might be denying patient access. Such a decision is contrary to the mission of public payers and is often complicated by public relations campaigning. The pricing policies of some manufacturers can therefore jeopardise both patient access and the sustainability of health systems.

For payers, the value, defined as added benefit compared to therapeutic alternatives (relative effectiveness), is one element in determining a "fair" price but it is not the only parameter for pricing decisions. Several pricing models are being developed, based on different concepts and/or algorithms for determining a fair price. These include models based on the incremental cost-effectiveness ratio (ICER), QALYs and the pricing model developed in 2019 by AIM[11]. The latter calculates a fair price by including the costs of R&D (taking into account the contribution made by public funds), production costs and logistics, and a bonus for the added value compared to therapeutic alternatives.

Finally, the net prices of medicinal products are often untransparent. The list prices of products are published but countries increasingly negotiate confidential discounts and pay lower net prices. Sometimes it is argued that confidential discounts are needed to allow less-wealthy countries to pay lower net prices. Nevertheless, separate, isolated, confidential price negotiations leave payers negotiating in the dark. It is known that in some case less wealthy countries are paying higher prices than wealthier countries, which can only be attributed to a lower negotiating power and the commercial strategy of the manufacturer. To increase their negotiating power, one of the strategies of payers has been to develop regional/national cooperations, as piloted by Beneluxa, Valetta-, Visegrad- (V4) and FINOSE. Besides conducting joint HTAs and horizon scanning activities, joint pricing negotiations have been part of these initiatives. To fully capture the potential of these initiatives adaptations to national legislations might be needed. However, the experiences gathered in regional collaborations can provide guidance for future processes for wider collaboration.

[10] https://www.oecd-ilibrary.org/docserver/5k43jc9v6knx-en.pdf?expires=1592317929&id=id&accname=guest&checksum=66A2FE1D772CD967D2B5024C54CA0007

[11] https://www.aim-mutual.org/wp-content/uploads/2019/12/AIMfairpricingModel.pdf

8. Actions for payers on European Level

	Payer Action	Goal	Collaboration with
1	Identifying high unmet medical need (lack of adequate treatment options, disease severity, rarity)	Prioritisation of new technologies that might be eligible for expedited authorisations and special support from payers	EMA, MAHs, health professionals and patient organisations
2.	Horizon scanning of technologies with potential major therapeutic advantage, assessing potential budget impact and expected costs	Anticipate emerging challenges and needs for pre- and post-launch actions to ensure patient access (especially for CMA)	EMA, EUnetHTA International Horizon Scanning Initiative (IHSI)
3.	(Participating in) early dialogues on evidence generation	Ensure the highest level of evidence possible pre- and post-launch, identify current comparators, identify targeted patient (sub-)populations	EMA, EUnetHTA, MoCA (Mechanism of Coordinated Access - a payer-manufacturer dialogue on access to medicines for orphan diseases)
4.	Assessment: supporting the development of methodologies to assess the added benefit of new technologies and using data from clinical practice	Methodologies for fundamentally new technologies and for evidence generation based on data from clinical daily practice	EUnetHTA, EMA
5.	Cost containment: discounts, financial Managed Entry Agreements	Budgets, price-volume contracts, expenditure limits per patient	Manufacturer
6.	Developing performance based MEAs linked to data generation	Access linked to evidence generation and adaptive pricing; identifying patient (sub-)groups, outcome parameters, obligations for participation etc.	Manufacturer, HTA, EMA, Registry holders
7.	Information strategies for patients and doctors	Awareness of the uncertainties linked to products with CMA and/or conditional reimbursement and the possibility of reimbursement withdrawal	EMA, HTA, patient organisations, provider organisations
8.	Possibly, developing new pricing models and establishing their legislative basis	Affordability and sustainability	National authorities, governments and national parliaments, European Institutions
9.	Cooperation between Member States; investigating new legislative options for regional cooperation	Enhanced transparency of prices, improved negotiating position	National governments and parliaments of existing regional cooperations (Beneluxa, Valetta-Visegrad- (V4), FINOSE)

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