



DELIVERING THE TRIPLE WIN:

A Value-Based Approach to Pricing



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Report Amendments

Amendments were made to Figure 1 in this report in February 2024 to correct discrepancies between Figure 1 and Table 3.

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Executive Summary

Pharmaceutical innovation is key to healthcare in the 21st century

In recent decades, healthcare has changed beyond recognition. Pharmaceutical innovations have improved life expectancy and quality of life (QoL) for patients around the world whilst also easing pressure on healthcare systems and contributing to the overall productivity of society. However, healthcare systems in Europe are also facing demographic pressures. Older people are the main users of medicines and other healthcare, and the share of the population aged 65 years and over is increasing in every EU member state (Eurostat, 2020). Pharmaceutical innovation has a critical role to play in helping healthcare systems adapt to this challenge. Breakthroughs in treatments for Alzheimer's disease, for example, could transform the expected trajectory of rapid increases in costs for dementia care in ageing societies (Braun et al., 2020).

A value-based approach to pricing supports sustainable innovation

The goal of pricing of pharmaceutical innovations is to ensure that patients can access medicines in a way that is sustainable for healthcare systems whilst also supporting a sustainable stream of innovation that delivers continuous improvements in the treatment options available for patients. Prices send signals to innovators about where to focus their R&D efforts, as well as determine the overall level of investment in health and expected value of innovation in the pipeline. This is why EFPIA is working with governments and stakeholders to identify and promote pricing approaches that deliver a 'triple win': ensure medicines are accessible, the healthcare system is sustainable, and the innovation pipeline is robust.

A value-based approach to pricing is based on the principle that prices should reflect the value of a new medicine to 1) patients, 2) health systems and 3) society versus the current standard of care. A value-based approach to pricing, therefore, means that healthcare systems appropriately reward innovation, and access to the most valuable innovations is prioritised. It also means that price signals are aligned with patients' and citizens' priorities, such that the expected value of innovation for a given level of investment is maximised. A value-based approach to pricing also ensures that the level of investment in pharmaceuticals, and level of expected innovation in the pipeline, reflects their value to society. Therefore, a value-based approach to pricing delivers the 'triple win': providing patients with access to the latest innovations, in a way which is sustainable for health systems, whilst ensuring that appropriate incentives exist to stimulate ongoing investment in the research and development of new treatments.

Any other pricing approach is less efficient in signalling what society values, and therefore incentivizing the right kind and amount and quality of innovation. In setting a rationale, shared, framework for rewarding innovation, a value-based approach to pricing serves as a useful starting point for policies designed to address related challenges, including how to ensure countries contribute fairly to rewarding innovation.

There is significant heterogeneity in how countries in Europe have implemented value-based approaches to pricing

A value-based approach to pricing is achieved through first, assessment of the value of a novel medicine and second, determining prices based on that value. Therefore, a value-based approach requires both that value is comprehensively assessed and that the results of value assessment are reflected in pricing and reimbursement (P&R) decisions and, ultimately, net prices¹.

Many countries in Europe have implemented aspects of value-based approaches to pricing. At the same time, however, many dimensions of the value generated by medicines – such as helping patients to return to work or improving the health and QoL of caregivers – are not consistently recognised in value assessment frameworks. Figure 1 shows which value elements are potentially recognised² in a country's value assessments, according to their health technology assessment (HTA) guidelines.

FIGURE 1: VALUE ELEMENTS RANKED IN ORDER OF HOW MANY COUNTRIES CONSIDER THEM IN VALUE ASSESSMENT

Considered in value assessment?	Yes	No
Health outcomes		
Cost of technology		
Other direct medical costs		
Treating severe diseases		
Direct non-medical costs		
Indirect non-medical costs		
Equity		
Health outcomes of carers		
Reducing unmet need		
Innovation		
Indirect medical costs		
Improvements in the process of care		
Treating rare diseases		

Key								
Belgium	France	Germany	Italy	Norway	Poland	Spain	Sweden	UK

It is important to note that some value elements may be recognised in HTA guidelines but not considered in appraisals in practice (Paris and Belloni, 2013a). In addition, some value elements are considered but only as part of 'additional' scenarios to be considered alongside the primary analysis - making it challenging to determine how much weight is given to them in appraisal. Finally, there is a lack of methodological guidance to facilitate inclusion of some value elements in practice.

A value-based approach to pricing requires not only that value is comprehensively assessed but that this value is then reflected in P&R decisions. Our research investigated whether nine countries in

¹ Net prices refer to the actual prices received by manufacturers, accounting for confidential discounts to the list price. A value-based approach to pricing requires that net prices reflect value.

² Including cases where there is ambiguity, which are discussed in the longer report.

Europe seek to align prices with value, and whether the use of alternative pricing approaches and price control measures disrupt this alignment (see Figure 2).

FIGURE 2: PRICING APPROACHES AND PRICE CONTROL MEASURES USED IN EUROPEAN COUNTRIES

Pricing approach or mechanism used?	Yes	No
A value-based approach to pricing		
<i>Alternative pricing approaches</i>		
Measures to control spending on individual products		
External referencing		
Measures to control total pharmaceutical budget		
Budget impact considerations		
Therapeutic referencing		

Key								
Belgium	France	Germany	Italy	Norway	Poland	Spain	Sweden	UK

All European countries considered in our research make some provision to reflect the results of value assessment in their P&R decisions. There may be a clear, mechanistic link, as in the case of countries using explicit cost-effectiveness thresholds, or a more deliberative and/or qualitative approach may be used.

We also note that a number of countries, including Germany and France, may implicitly recognise the value of treatments for very rare diseases through an exemption to value assessment for products receiving Orphan Medical Product (OMP) designation (when their budget impact is expected to be below specified thresholds). Demonstrating value can be challenging for treatments for very rare diseases, in part due to the small patient populations able to participate in clinical trials. The OMP exemption can ensure faster patient access to treatments in areas of high unmet need, where value is challenging to estimate but the potential to deliver value to society is high (and the budget impact is low). However, value is not precisely aligned with price.

All countries considered in our research also make use of other pricing approaches or price control measures that disrupt the alignment between value and price, meaning that many of the benefits of a value-based approach to pricing will not be realised. Seven countries use external referencing, which is not only inconsistent with the principles of value-based approaches to pricing but may also be associated with patient access delays. In addition, seven countries employ further measures such as clawbacks (where innovators pay back revenue if spending on pharmaceuticals exceeds a certain threshold) to control the total pharmaceutical budget, which means that the investment incentives provided by a value-based approach are undermined.

Although empirical evidence is limited, there are indications that the value societies place on health is underrecognized in spending on healthcare. For example, there is evidence from Sweden and the UK that sectors such as transport implement higher thresholds for life-saving interventions (Elin et al., 2022; Persson, 2018; HM Treasury, 2022). Greater utilisation of novel medicines and investment in pharmaceutical innovation are therefore expected to improve the welfare of patients and society.

Making a value-based approach pricing work in Europe for patients, healthcare systems, and innovations

On the basis of our research, we have developed a number of recommendations which can enhance how value-based pricing approaches are implemented, for the benefit of all stakeholders.

Enhancing value assessment and recognition

Recommendation 1: ensure meaningful involvement of stakeholders in value assessment and recognition. Involvement of stakeholders including patients, clinicians and carers in value assessment and recognition processes is crucial for ensuring that all perspectives on the value of novel medicines are captured and appropriately integrated into valuation and P&R decisions. Involvement of innovators at an early stage in the value assessment and recognition process is also important for facilitating discussion about which evidence should be collected during drug development in order to facilitate a comprehensive assessment of value. Innovators and value assessment bodies should invest in earlier and more frequent pre-launch cooperation, for example, through increased development and engagement with joint scientific consultations.

Recommendation 2: develop a shared and holistic definition of value. Stakeholders should also work together at the country-level to develop a joint, shared and holistic definition of value that recognises the multiple dimensions of value that novel medicines generate for patients, healthcare systems and society. This would ensure that R&D effort is directed where a country's society values most. It would also provide a starting point for collaboration between stakeholders on evidence and methods development, and for discussions about how the value generated by innovation could be shared to help healthcare systems navigate affordability challenges.

Recommendation 3: enhance collaboration and share expertise across EU Member States. Fully embracing a fit-for-purpose system of joint clinical assessment at the EU level (as foreseen by the EU HTA Regulation) will allow for a more efficient use of resources and a more aligned view on the clinical value of a medicine across the EU, thus ensuring more capacity at a national level for a differentiated and context-specific analysis of the value of the medicine in respective societies. Appropriate resourcing of joint EU clinical assessment will be important to deliver on these benefits.

Recommendation 4: recognise qualitative evidence of value through deliberative processes Recognition of qualitative evidence of value is important for progressing towards more comprehensive value assessment and can provide concrete incentives for innovators to make R&D decisions in line with a more holistic definition of value. Many value assessment bodies already recognise value qualitatively when quantitative evidence is lacking. Deliberative processes for value assessment, a form of structured-decision making, provide a mechanism for explicitly and rigorously assessing the value of novel medicines through the systematic consideration of heterogeneous arguments and evidence, including qualitative evidence (Oortwijn et al., 2022; NICE, 2022a).

Embracing a value-based approach to pricing

Recommendation 5: fully embrace a value-based approach. Value-based approaches require that net prices are aligned with value, and the use of alternative pricing mechanisms disrupts this alignment. We recommend that countries should fully embrace a value-based approach, by avoiding the use of alternative pricing approaches.

Recommendation 6: extend a value-based approach to the indication level. An indication-based approach to pricing, where prices for the same medicine vary according to the value generated in treating different indications, refines the signals sent to innovators by facilitating an even more specific alignment between price and value. It also generates incentives for manufacturers to invest

in developing novel medicines for new indications for which they are effective and safe. Whilst there are practical challenges to implementing value-based approaches at the indication level, there also are examples of how countries such as France and Italy have begun to operationalise some elements of an indication-based approach to pricing (Towse, Cole and Zamora, 2018; Flume et al., 2016).

Complementing value-based approaches with other tools

Recommendation 7: use outcomes-based managed entry agreements to manage residual uncertainty. There are a number of payment models that can facilitate value-based approaches in the context of uncertainty surrounding outcomes. Many countries already make use of outcomes-based managed entry agreements, and this could be extended through early dialogue between stakeholders to resolve challenges around defining (surrogate) outcome measures and measuring performance.

Recommendation 8: enhance data collection infrastructure to allow for iterative assessments of value post-launch. Holistic data collection and analysis across healthcare systems can enable more tailored assessments of value delivered in real-world settings (including for monitoring novel payment models and for managing uncertainty). Metrics for measuring different dimensions of value, including health outcomes for patients, should be standardised in order to increase comparability and reliability, building on the joint definitions of value developed by all stakeholders. Additionally, such visibility also allows manufacturers to better focus R&D efforts in areas where value for healthcare systems can be delivered better.

Recommendation 9: commit to 'Equity Based Tiered Pricing'. A value-based approach to pricing can help to ensure that the level of investment in pharmaceutical innovation – and quality and quantity of the innovation pipeline – reflect the value of innovation to society. However, it does not solve the challenge of how investment in innovation should be distributed between countries, given there are incentives at the country-level to underinvest. EFPIA has therefore proposed a conceptual framework for 'Equity Based Tiered Pricing' (EFPIA, 2022). This builds on the principles of value-based approaches to pricing, with countries negotiating confidential value-based prices based on their own value assessments, but introduces a "best price rule", whereby innovators commit to ensuring that less wealthy EU countries in the "lower tier" pay less than wealthier countries in the "upper tier".

Recommendation 10: promote competition. A value-based approach to pricing works in synergy with a competitive market for medicines, to deliver healthcare system sustainability. Indeed, value-based pricing itself promotes product competition; it increases the expected number of innovations in the therapeutic areas prioritised by society and, since rewards for innovations are in-line with the improvements they offer on existing alternatives (society will only pay for more value), innovators are incentivized to develop substantial improvements (Roediger et al., 2019; Berdud et al., 2018). There are additional, complementary tools available to policymakers for strengthening competition.

Conclusion

A value-based approach to pricing will help to deliver a sustainable stream of innovation, delivering the 'triple win' and so benefits patients, healthcare systems, and payers. Whilst many countries in Europe recognise the potential of a value-based approach, and experiment with its implementation, there is significant heterogeneity in how far this has been done and to what extent other pricing approaches act to disrupt the alignment of value and price. There are many opportunities to improve how a value-based approach to pricing is implemented for the benefit of all stakeholders, and this is what we seek to encourage through our recommendations.

Introduction

In recent decades, healthcare has changed beyond recognition. Pharmaceuticals have improved life expectancy and quality of life (QoL) for patients around the world, whilst also easing pressure on healthcare systems and contributing to the overall productivity of society. Where previously hepatitis C patients' only hope of treatment was liver transplantation, followed by life-long use of immunosuppressants, 95% of the 15 million people living with hepatitis C in Europe can now be cured through an 8 to 12 week course of treatment with direct-acting antivirals (EFPIA, 2015). Between 2000 and 2012, the death rate from cardiovascular disease in the EU4 and the UK reduced by 37%, thanks in part to new treatments that have revolutionised the way we manage high cholesterol (EFPIA, 2015). These new treatments have also freed up healthcare system resources: per capita expenditure on cardiovascular hospitalisations would have been 70% higher in 2003, had new cardiovascular medicines not been introduced between 1995 and 2003 (EFPIA, 2015).

Case Study 1: innovation in cancer treatments

In oncology, a total of 64 new active substances have launched globally in the last 5 years, bringing the 20-year total to 161 (IQVIA, 2021). In 1996, a physician had only four medicines to treat lung cancer; in 2016, there were 19 different medicines available (Aitken, Kleinrock and Kumar, 2017). Advances in cancer treatments have helped to improve 5-year metastatic skin cancer survival from 5% (2009) to over 50% (2019) over the past decade (ESMO, 2019). Over the past fifteen years, the 5-year survival rate for patients with chronic myeloid leukaemia has improved from less than 20% to more than 90%, thanks to the advent of a class of drugs known as tyrosine kinase inhibitors (TKIs) (Kantarjian et al., 2012).

However, healthcare systems in Europe are also facing demographic pressures. Older people are the main users of medicines and other healthcare, and the share of the population aged 65 years and over is increasing in every EU member state (Eurostat, 2020). The 'old age dependency ratio' (the number of people over 65 divided by the number of people of working age) in the EU increased from 26.6% in 2011 to 32.5% in 2021 (Eurostat, 2022). Pharmaceutical innovations have a critical role to play in helping healthcare systems adapt to this challenge. Breakthroughs in treatments for Alzheimer's disease, for example, could transform the expected trajectory of rapid increases in costs for dementia care in ageing societies (Braun et al., 2020).

Prices of novel medicines (innovative molecules in the intellectual property protection phase of the medicine's life cycle) send signals to innovators about where to focus their research and development (R&D) effort, and to investors about how much and where to invest in the research-based pharmaceutical industry. Therefore, the pricing approaches in use in healthcare in Europe and worldwide influence the attractiveness of investment in pharmaceutical innovation, and in turn, the strength of the innovation pipeline. A value-based approach to pricing is founded upon the principle that prices reflect the value of a novel medicine to patients, healthcare systems, and society versus the current standard of care. EFPIA's position is that a value-based approach to pricing, when well-designed and applied, is the optimal pricing mechanism through which governments and healthcare systems can navigate the challenges outlined above. This is because it delivers a sustainable stream of investment into pharmaceutical innovation that reflects the value of health to society and sends efficient price signals to innovators, which ensures that investment is directed towards citizens' priorities.

This position paper advocates for a value-based approach to pricing; explores how countries in Europe have implemented this approach to date; and presents recommendations for improving how value-based approaches are implemented, for the benefit of all stakeholders.

1. How a value-based approach to pricing supports sustainable innovation

Key messages:

- The goal of pricing of pharmaceutical innovations is to ensure that patients can access new medicines in a way that is sustainable for healthcare systems, whilst also supporting a sustainable stream of innovation.
- A value-based approach to pricing is based on the principle that prices should reflect the value of a new medicine to 1) patients, 2) health systems and 3) society versus the current standard of care.
- A value-based approach to pricing, therefore, means that healthcare systems appropriately assess and reward innovation, and access to the most valuable innovations is prioritised.
- Prices send signals to innovators about where to focus their R&D efforts, and therefore a value-based approach to pricing ensures that these efforts are aligned with patients' and citizens' priorities.
- A value-based approach to pricing ensures that the level of investment in health, and level of expected innovation, reflects its value to society.
- In setting a rational shared framework for rewarding innovation, a value-based approach to pricing serves as a useful starting point for policies designed to address related challenges, including how to ensure countries contribute fairly to rewarding innovation, ensuring continued investment in R&D
- A value-based approach to pricing delivers the 'triple win': providing patients with access to the latest innovations in a way which is sustainable for health systems whilst ensuring that appropriate incentives exist to stimulate ongoing investment in the research and development of new treatments.
- Any other pricing approach is less efficient in signalling what society values and, therefore, incentivizing the 'right kind' of innovation. Not only this, but other pricing approaches can create access and affordability challenges for healthcare systems today.

This section introduces the concept and core principles of a value-based approach to pricing and explains its unique benefits compared to other pricing approaches. First, however, we provide a brief introduction to pricing in the pharmaceuticals market.

1.1 Pricing in pharmaceutical markets

Pharmaceutical markets differ from 'traditional' markets in that they are highly regulated. Market access depends on meeting stringent safety regulations, and in single-payer markets, public healthcare purchasers or insurers act on behalf of the consumers of pharmaceuticals ("patients"), functioning as monopsony health buyers. In addition, intellectual property protection provides a mechanism for innovators in the research-based pharmaceutical industry to recoup their R&D investments before their innovations are copied, and pharmaceutical innovators, therefore, act as monopolist sellers during this period. As a consequence, prices of novel medicines in the intellectual property phase of their life cycle are determined through negotiation between monopsony purchasers and monopolist sellers.

Why are novel medicines protected by intellectual property rights?

The market for novel medicines, as for other research-intensive products, is characterised by a number of well-recognized inefficiencies. In particular, innovators must invest substantial resources to develop a product from scratch (with high risk of failure), but subsequent sellers can avoid these costs by ‘copying’ (at very low cost) the original innovation, allowing them to sell the same product for substantially less than the innovators’ break-even price and still obtain substantial profits. Moreover, new pharmaceuticals need to be approved by regulators, e.g., FDA, EMA, for their human use. Originators bear the risk of this approval stage, while copied versions face either minimal regulatory hurdles (generics) or much lower requirements for their approval (biosimilars). In the absence of policy to correct these inefficiencies, it is difficult or impossible for innovators to compete in selling their own inventions, and the incentives for innovation are fundamentally undermined. Intellectual property rights like patents and market exclusivities address these challenges by granting temporary exclusive rights to the innovator, who therefore has an opportunity to make a return on their investment. They do not, however, prevent competition from other products, such as similar or more efficacious treatments for the same condition.

In pricing negotiations, healthcare purchasers seek to minimize costs, in order to maximise the amount of health they can buy for a fixed budget. Indeed, “static efficiency”, or the health which can be consumed at a fixed point in time, is maximised when prices are equal to marginal costs. After the expiration of intellectual property rights, cost minimisation may be a healthcare purchasers’ only goal. In markets for novel medicines, healthcare systems seek to minimize costs and therefore maximise patient access to the latest innovations, but also have a responsibility to citizens to encourage a sustainable stream of investment in the pharmaceutical industry, by rewarding innovation sufficiently and sending price signals that direct R&D efforts to the areas that citizen’s value. Given that healthcare purchasers operate under constrained budgets, they therefore face a trade-off between dynamic efficiency (total expected health over-time) and static efficiency in the market for novel medicines. In addition, in the global market for medicines, individual healthcare purchasers have incentives to free-ride on the incentives for innovation offered by others (Danzon and Towse, 2003). The theoretical economic prediction is, therefore, that purchasers tend to underinvest, relative to how much they (acting on behalf of the citizens they represent) value health.

From the perspective of innovators, intellectual property protection exists to enable them to earn a return on the R&D investment involved in bringing an innovation to market - since after it expires, their innovation can be copied. Pharmaceutical innovators seek to develop novel medicines which improve patients’ health and bring benefit to society, and their negotiating objective is to obtain a price which rewards that value. Healthcare purchasers and innovators negotiate to reach mutually acceptable prices, and a ‘pricing approach’ is a set of principles used to guide this process.

1.2 The rationale for value-based pricing

The goal of the pricing of novel medicines is to deliver the ‘triple win’: ensuring that patients can access new treatments, in a way that is sustainable for healthcare systems, whilst also supporting a sustainable stream of innovation. Intellectual property rights exist to promote investment in medical R&D, which would otherwise be below the social optimum, by providing a temporary means for innovators to be rewarded for their innovation (Bryan and Williams, 2021). A value-based approach to pricing starts from the simple and unique principle that these rewards should be aligned with the value of innovation, compared to the current standard of healthcare. In this way, the most valuable new innovations are prioritised, and innovators R&D efforts are directed towards developing the pharmaceutical innovations that are expected to be most valuable to society.

What is value in health and why is it important to measure it?

The pharmaceutical industry's main ambition is to develop and produce innovations that help patients live longer and better lives. It is also increasingly recognised that pharmaceutical innovations are valuable to healthcare systems and to society more broadly. For example, when a patient is cured of a disease, the resources previously needed to manage their condition can be invested in other forms of healthcare, and the psychological and physical burdens on their caregivers are eased.

Whilst what is valuable to patients and populations more broadly is inherently subjective, and thus context-dependent, a number of value frameworks have been proposed to conceptualise the many dimensions of value which can arise from pharmaceutical innovations and healthcare in general (see, for example, Lakdawalla et al. (2018) and Rothery et al. (2018)) and there exists a lively academic debate on the definition of value in health. One simple tool for articulating the value of pharmaceutical innovations is EFPIA's core value framework (EFPIA, 2019b), which conceptualises value in terms of three dimensions:

- **Value to patients:** improvements in patients' health, for example, increased cure rates, quality of life, and/or length of life. Patients may also value the process by which a treatment is delivered: a pill compared to a transfusion, for example, may save them discomfort, as would decreased travel time to a healthcare provider.
- **Value to healthcare systems:** effects on the resources required by the healthcare system in providing treatment. For example, a novel medicine may offer value if it replaces a more expensive (or equally expensive but less effective) alternative, or if it means that fewer resources are needed to provide ongoing care (including social care) for the patient or to treat complications from chronic conditions or diseases (European Commission, 2019).
- **Value to society:** there are many other ways in which novel medicines and other health technologies may offer value to society. For example, vaccinations can provide herd immunity. Novel medicines can ease ill-health caused by psychological and physical burdens on caregivers; enhance productivity when patients and caregivers can either return to work or minimise personal and societal costs of using sick or compassionate leave; and contribute to environmental sustainability (i.e., through green manufacturing practices). Novel medicines also produce scientific spillovers, which are extremely valuable to society because they enhance the quality of future innovations in healthcare and attract industrial investments - boosting economic growth and employment.

Different societies may value different dimensions of value, to different extents. A value-based approach to pricing requires that societies (or policymakers acting to represent them) can define the value that novel medicines generate and have an approach to measuring this.

Defining and measuring value is important not only for a value-based approach to pricing, but because it facilitates prioritisation in the healthcare system. Imagine, for example, a novel medicine which involves an innovation in delivery: treatment is provided via a slow-release patch rather than a daily pill. The slow-release patch might have identical results to the daily pill in a clinical trial, but in the real world would improve patients' adherence and, as a result, their health outcomes. Without a definition of value which incorporates the value of process innovations and an approach to value assessment which measures this value, the benefits of the novel medicine will not be recognised or incorporated into decisions about which treatments to prioritise.

Prices not only send signals to innovators about where to invest but – together with the length of intellectual property rights and the market size for a product – determine the returns to innovation, and, therefore, the level of investment in pharmaceutical R&D and level of expected innovation in the

pipeline. A value-based approach to pricing also helps to ensure that these rewards reflect the value of healthcare innovations to society and, therefore, will deliver the pipeline of innovation that society wants. Indeed, dynamic efficiency (total societal welfare over time) is maximised when prices equal societies' willingness-to-pay for innovations, and the length of intellectual property rights is optimally designed (Danzon and Towse, 2003). A value-based approach to pricing has the additional advantage of providing a predictable, shared approach for rewarding innovation. This gives producers confidence to invest in long and risky R&D projects and maximises the chances that consumers and producers can agree mutually beneficial prices, thereby contributing to timely patient access and to on-patent competition between treatment options.

By aligning the incentives of innovators with those of society, a value-based approach to pricing provides a mechanism for delivering a sustainable stream of pharmaceutical innovation and sends efficient price signals that maximise the expected value of that innovation. In providing a rational set of incentives for innovation, a value-based approach to pricing also offers a useful starting point for evidence-based policies that address related challenges. We have already noted that healthcare systems with budget constraints face a trade-off between dynamic and static efficiency. Whilst no pricing approach can change these budget constraints, a value-based approach to pricing contributes to improved understanding and evidence about how pharmaceutical innovation generates value for society, and in turn how this value might be "shared" to help healthcare systems manage affordability challenges. Similarly, a value-based approach to pricing does not eliminate incentives for healthcare purchasers to free-ride, but it does provide a baseline for "Equity Based Tiered Pricing", a set of principles anchored in solidarity between countries which seeks to ensure that ability to pay across countries is considered in the value-based pricing of novel medicines (EFPIA, 2022). In section 3, we provide recommendations for enhancing the implementation of value-based approaches, as well as recommendations on these complementary policies.

A value-based approach to pricing delivers the 'triple win': providing patients with access to the latest innovations, in a way which is sustainable for health systems, whilst ensuring that appropriate incentives exist to stimulate ongoing investment in the research and development of new treatments.

1.3 Other pricing approaches

This section provides a brief introduction to three other approaches to the pricing of novel medicines which are implemented or proposed by European countries. All these approaches fail to align the incentives of pharmaceutical innovators with those of society, and so the quality of innovation in the pipeline is expected to be lower than under a value-based approach to pricing. This means less competition in the therapeutic areas that society values the most, and from a dynamic perspective, patient access and healthcare system sustainability are therefore also expected to be compromised compared to a value-based approach to pricing. We also show how some alternative pricing approaches create immediate access and sustainability challenges, either in the countries implementing them or internationally.

Therapeutic referencing (TR): TR places medicines to treat the same medical condition into groups or 'clusters' with a single common reimbursed price. Medicines considered to offer a sufficiently high level of innovation in comparison to other available treatments may be exempt from TR, or, be awarded a premium on top of the reference price. When prices are set with reference to what has historically been agreed for other medicines in the same cluster, they may bear no relation to value. There are therapeutic referencing approaches that recognise value, through cost-effectiveness analysis or the use of premiums to reward therapeutic value added that try to link the value of innovation to the price, but they are often blunt or combined with tools to control budget impact, such as budget impact thresholds (Sheridan and Attridge, 2006). In comparison to a value-based

approach to pricing, it is expected that healthcare systems using TR would allocate resources less efficiently (meaning less health can be purchased with constrained budgets) as a higher proportion of the healthcare system budget may be spent in clusters that provide relatively less value than if the medicines were priced based on their individual value. In addition, the quantity of innovation in high-value therapeutic areas and, therefore, the level of competition in these areas, would be lower. If additional value is not reflected in prices, the incentives for innovators to develop products with relatively higher value are reduced.

External referencing (ER): external referencing is the practice of benchmarking the price of a product using the prices paid for the same product in other countries. A country defines a basket of countries according to characteristics, such as gross domestic product, population size and willingness to pay, and use their prices for a product to generate a benchmark. This benchmark can reflect the average, minimum or maximum price paid by other countries in the basket, or some other measure. It can determine the actual price paid or operate as a minimum or maximum price cap.

ER may be used by countries as a tool for managing financial sustainability or, alternatively, as a practical pricing approach when they lack capacity to implement value assessment and, therefore, to implement a value-based approach to pricing. The use of ER is associated with inefficient behaviours and, as a result, outcomes. For example, countries may strategically include in their basket other countries which have greater negotiating power, cap prices, or have lower ability to pay. However, in doing so, ER can create access delays in those countries which are likely to be included in reference baskets. Evidence suggests that ER contributes to innovators' reluctance to sell at low prices, especially in small, lower-income countries in the EU, because low prices in any EU country can undermine potentially higher prices in other EU countries (Danzon, 2018b). Not only this but by promoting price convergence, ER undermines the principle that richer countries with a higher willingness to pay for health should contribute more to rewarding innovation thereby ensuring continued investment in R&D, which is essential for equitable global access.

ER is also expected to have negative implications for the countries implementing it. It is an inefficient price-setting mechanism because it outsources decisions about what the healthcare system is willing to pay for a novel medicine to other countries (Kanavos et al., 2020). These countries may not base their pricing on assessment of value or may value the medicine differently due, for example, to different population structures or disease burdens. In comparison to a value-based approach to pricing, it is expected that healthcare systems using an ER approach to pricing would allocate resources less efficiently. The expected quantity and quality of future innovation and level of competition between medicines would also be lower due to the weaker alignment between value and price. Countries use of ER pricing also compromises timely access globally, with countries included in ER baskets facing the risk of the longest delays in accessing innovation.

Cost-plus pricing (CPP): CPP is the principle of setting the price of a product based on its costs of production plus a profit margin (for example, a percentage of the costs of production, or a fixed profit). When estimated for CPP purposes, costs of production typically include manufacturing costs, costs associated with regulatory processes and compliance, and overhead and other operational expenses (World Health Organization, 2020). Typically, the payer determines the acceptable mark-up or profit margin it considers "fair" – or sufficient to reward an appropriate fraction of global R&D investment.

CPP may be viewed as a tool for managing healthcare system sustainability, because, in theory, it provides a one-shot 'windfall' to payers by lowering the prices of products to their cost of production, even during patent protection. There are no agreed methods for ascertaining the costs of R&D, and any attempts to do so require so many assumptions as to produce very arbitrary estimates (Morgan, 2016; Schlender et al., 2021). Therefore, this crucial portion of the cost of producing innovation is either neglected or not accurately estimated. This is because scientific spillovers are unobservable

and not feasible to accurately quantify (European Commission, 2019) for several reasons. Firstly, it is unfeasible to link early-stage R&D investment to specific launched products. Secondly, it is unfeasible to adjust by the cost of failures unless it is done, at least, at firm level failures or therapy area average, and finally, because in the best case, if the figure can be estimated, it is difficult to apportion global R&D investment to different countries in a fair way (Henderson and Cockburn, 1996; Wong, Siah and Lo, 2019; DiMasi, Grabowski and Hansen, 2016).

Leaving aside these technical challenges, CPP is fundamentally flawed because it misdirects the incentives of innovators towards investing in those areas which are most profitable given the design of the cost-plus approach (for example, the areas with the highest R&D costs or the lowest risk of failure). CPP also incentivizes inefficiency: there are no rewards to innovators for streamlining their R&D processes, especially if higher R&D costs translate to higher prices (Schlander et al., 2021). This means that less efficient innovators have a profit-making advantage, with negative implications for sustainability (beyond the initial windfall when CPP is first introduced) and overall societal welfare (as societies' resources are used inefficiently). Not only this, but in comparison to a value-based approach to pricing, it is expected that healthcare systems using CPP would allocate resources less efficiently and that the quantity and quality of innovation and level of competition between novel medicines would be lower. Finally, as with ER, CPP promotes price convergence, and so its use would either create access and financial sustainability challenges for lower-income countries in the EU and globally or substantially undermine incentives for innovation.

2. Experiences implementing a value-based approach to pricing in Europe

In this section, we explore the implementation of a value-based approach to pricing in Europe. We analyse the extent to which a value-based approach to pricing has been implemented in a sample of nine European countries and identify outstanding challenges facing healthcare systems and innovators seeking to apply value-based pricing principles. We frame our analysis around two questions:

Is value comprehensively assessed? A necessary precondition of a value-based approach to pricing is that the bodies who make P&R decisions have a comprehensive understanding of the value offered by health technologies. However, health technology assessment (HTA) bodies often face practical and methodological challenges in defining and measuring value.

Are higher-value products rewarded with higher prices? A value-based approach to pricing requires that the results of value assessment are reflected in pricing decisions. Use of alternative price-setting mechanisms to determine the list price, as well as cost-containment measures such as discount and expenditure caps which can affect the effective, net price, can distort the alignment between price and value.

Key messages:

- Although empirical evidence is limited, there are indications that the value societies place on health exceeds the level of public investment in healthcare systems in general and in particular, novel medicines.
- Greater utilisation of novel medicines and investment in pharmaceutical innovation are therefore expected to improve the welfare of patients and society – even without considering the value beyond health that novel medicines generate.
- Many countries in Europe have implemented aspects of value-based approaches to pricing, to a lesser or fuller degree.
- However, many dimensions of the value generated by medicines – such as helping patients to return to work or improving the health and quality of life of patients and caregivers – are not consistently recognised in value assessment frameworks.
- In addition, the use of other pricing approaches (such as external referencing) and measures to control spending on novel medicines disrupts the alignment between price and value – meaning that many of the benefits of a value-based approach to pricing will not be realised.

2.1 Context

2.1.1 Value assessment

An increasing number of countries in Europe have established dedicated health technology assessment (HTA bodies), which are responsible for assessing (and reassessing) the value of health technologies. Perhaps due to the many dimensions of value, and ways in which they can be evidenced, HTA bodies also employ a range of methodologies for value assessment (EFPIA, 2019a), with variable standards for which evidence can be included and methods for managing uncertainty. The case study of orphan medicines illustrates both some of the challenges which novel medicines have posed to value assessment systems, and the progress countries in Europe have made to address these.

Case Study 2: value assessment of orphan medicines

WHAT ARE ORPHAN MEDICINES?

The number of people suffering from an individual rare disease is, of course, small but overall, rare diseases affect many Europeans (Aartsma-Rus, Doods and Le Cam, 2021). About 30 million people in the EU, or 6% of the population, suffer from rare diseases (Wakap et al., 2020). An estimated 80% of rare diseases are of genetic origin and are chronic and life-threatening (Aartsma-Rus, Doods and Le Cam, 2021) and for 95% of rare diseases there is no authorised treatment available (Tambuyzer et al., 2020). The small number of patients affected by individual rare diseases means that the commercial market for treatments for rare diseases is also small. It also makes research and clinical trials more challenging and riskier; regulatory approval more difficult to achieve; and, overall, limits the investment case for novel medicines for rare diseases (Aartsma-Rus, Doods and Le Cam, 2021). Recognising that “[developing] medicines intended for small numbers of patients has little commercial incentive under normal market conditions” (European Medicines Agency, 2020), the EU introduced a regulation in 2000 designed to increase the availability of “orphan medicinal products” (OMPs): treatments offering significant benefit or addressing unmet need for life-threatening or chronically debilitating, rare diseases.

The OMP Regulation introduced a specific set of incentives for designated OMPs: a 10-year market exclusivity period, protocol assistance from the European Medicines Agency (EMA), fee reductions during the approval process, and EU-funded research for OMP development aimed at increasing research in rare diseases (Aartsma-Rus, Doods and Le Cam, 2021). Evidence suggests that the OMP regulation has been effective in increasing the availability of OMPs: recent research indicates that over half (74) of the OMPs authorised between 2000 and 2017 would not have been economically viable in the absence of the Regulation (Dolon, 2020). However, the increased availability of OMPs has also posed challenges for value assessment bodies, and investment in R&D of treatments for the rarest diseases remains low (Aartsma-Rus, Doods and Le Cam, 2021).

WHAT ARE THE CHALLENGES OF VALUE ASSESSMENT OF OMPs?

Traditionally, frameworks for value assessment have not been well suited to the type and level of evidence that can feasibly be collected in the OMP environment (Aartsma-Rus, Doods and Le Cam, 2021). Small population sizes mean that OMP trials are often characterized by a smaller evidence package available at the time of regulatory approval compared to non-orphan drugs, and greater treatment effects or longer trial duration are required from small-scale trials to attain statistical significance unless innovative trial designs are used (Nicod et al., 2017).

In addition, there are several dimensions of value associated with OMPs that historically have been either partially or entirely unrecognised in value assessments (Berdud et al., 2020). For example, there is substantial evidence that carrying out caring duties or being the family member of an ill relative, can have a significant negative impact on health and QoL (Wittenberg, James and Prosser,

2019). The size of these ‘family spillovers’ is expected to be particularly large for OMPs because of the severity and chronic nature of rare diseases; the frequency with which they occur in children; and the complexity of some rare diseases (which can involve multiple organs and so are difficult to manage) (Berdud et al., 2020). A study in Italy carried out by Neri et al. (2016) found that 34% of the parents of children with cystic fibrosis reported short depression–happiness scale scores suggestive of clinical depression (Neri et al., 2016). A study in Spain reported that the estimated average EQ-5D score (a well-known and used generic measure of quality of life) for Spinal Muscular Atrophy caregivers was 0.49 while that of the general population of the same age was 0.959 (López-Bastida et al., 2017). Just as the health spillovers to family members are expected to be particularly large for OMPs, so too are the impacts on caregivers’ and family members’ productivity (Berdud et al., 2020).

Other dimensions of value, such as scientific spillovers from developing novel treatments in areas of unmet need; equity in the distribution of health; the value of treating more severe diseases are also likely to be larger on average for OMPs compared to non-orphan medicines (Berdud et al., 2020; Shafrin et al., 2021). If these dimensions are indeed valuable to society but are not included in value assessments, OMPs are, therefore, likely to be undervalued relative to other treatments, leading to below-optimal resource allocation and incentives for innovation for OMPs.

Furthermore, this undervaluation can lead to a perception that the prices of OMPs – which must allow innovators to generate (expected) attractive returns across a small patient population – are ‘high’ compared to prices for other novel medicines. More comprehensive and accurate value assessment would demonstrate the value that OMPs generate for patients, caregivers, healthcare systems, and the general population – and therefore reassure society that a fair price is being paid for these treatments.

HOW HAVE COUNTRIES RESPONDED TO THE CHALLENGE OF ASSESSING THE VALUE OF OMPs?

Countries have responded to the challenges of assessing the value of OMPs in a variety of ways. For example, France has introduced specific evidentiary requirements for OMPs, and may consider a small trial population and noncomparative trial acceptable if the number of patients living with the disease is very low (Nicod et al., 2017).

In the UK, NICE introduced a designated value assessment process for ‘ultra-OMPs’ (for diseases affecting less than 1 in 50,000 people), the Highly Specialised Technologies (HST) programme, in 2013. OMPs assessed through the HST programme could be found cost-effective at an incremental cost-effectiveness ratio (ICER) of up to £300,000 per quality adjusted life year (QALY)³ compared to the conventional threshold of £20,000-30,000/QALY, on the basis that society places more value on treatments for rare conditions and with higher ‘magnitude of benefit’ (NICE, 2013). Sweden has also begun to consider rarity as a justification for acceptance of a higher ICER threshold (Nicod and Whittal, 2020). In section 3, we explore how value assessment of OMPs is continuing to evolve.

Despite progress in value assessment in Europe over recent years, the heterogeneity in value assessment processes and methods creates several inefficiencies. For innovators, duplicative administrative work is required. For HTA bodies, there can be an inability to conclude assessments based on the evidence provided, because the evidence was generated for other purposes and does not fit national requirements. Most importantly, for patients, the lack of methodological alignment means unnecessary trials, potential delays, and access restrictions (EFPIA, 2019a).

Joint European value assessment offers the opportunity to substantially reduce these inefficiencies. Progress on joint value assessment has been made by the European Network for HTA (EUnetHTA), which was set up in 2006 to promote more collaboration and harmonisation in the EU, by linking national HTA agencies, research institutions and health ministries. EUnetHTA has conducted a

³ The QALY is a summary measure of mortality and morbidity, commonly used to measure health benefits in value assessment.

number of pilots which demonstrate the feasibility of joint assessment of the clinical value of health technologies (EFPIA, 2019a). However, a number of barriers persist, including discrepancies between EUnetHTA and national HTA body methodologies and timelines for value assessment (in countries including Italy and the Netherlands, waiting for the publication of the final EU report would delay the national HTA process for most health technologies (Wilsdon, Pistollato and Li, 2017)). In some countries, changes will also be required to national laws and regulations for value assessment to realise the benefits of joint European value assessment. In Germany, for example, current rules require the national HTA agency to accept value assessments commissioned only from national agencies; in Poland, changes in legislation would be required to allow joint EU assessments to replace part of the national assessment, instead of being used as an additional input (Wilsdon, Pistollato and Li, 2017).

Recognising that substantial variation still exists in the value assessment methodologies employed by HTA bodies in Europe, the first objective of our analysis is to explore how comprehensively value is assessed across a range of European countries. Specifically, we consider how extensive the coverage of 13 distinctly defined 'elements' of this value is by assessing HTA bodies' guidelines, and the extent to which these guidelines facilitate value assessment in the context of uncertainty (see section 2.3.1). In section 3, we explore potential policy options for enhancing the comprehensiveness of value assessment, including through joint EU value assessment.

2.1.2 A value-based approach to pricing

Whilst comprehensive value assessment is a necessary precondition of a value-based approach to pricing, it is not sufficient. A value-based approach to pricing requires that the results of value assessment are reflected in P&R decisions: that the reimbursement and net prices medicines of medicines align with their value. An increasing number of P&R bodies in Europe state that they seek to reflect the results of value assessment in P&R decisions. However, other considerations, such as budget impact, the prices paid for comparable products, and the prices paid for the same medicine in other countries continue to influence the list prices agreed for innovative medicines. Moreover, the use of cost containment measures, which may be applied either at the product level or to pharmaceutical budgets more broadly, can lead to further divergence between the value-based price and the net price. The second objective of our analysis is to assess whether countries in Europe apply value-based principles when making P&R decisions, and whether the use of other pricing approaches (specifically those which are counter to the principles of a value-based approach to pricing) and price control measures disrupts the alignment between price and value (see section 2.3.2).

2.1.3 Managing uncertainty in value assessment, pricing and reimbursement

The ability of value assessment and P&R bodies to manage uncertainty is increasingly important to facilitate timely patient access to treatments, at prices which are aligned with value. This is due to recent innovations in areas such as precision medicine and rare diseases, which are associated with particularly high levels of uncertainty due to uncertain treatment pathways and small patient populations, respectively. Some value assessment bodies have adapted to this challenge through, for example, use of surrogate endpoints and real-world evidence. European P&R bodies are also increasingly making use of innovative payment models such as outcomes-based managed entry agreements (MEAs), which can facilitate access to promising but uncertain treatments whilst ensuring that the price ultimately paid is aligned with value. The third objective of our analysis is to assess the extent to which countries in Europe have adopted strategies to manage uncertainty in value assessment and P&R (see section 2.3.3).

2.2 Methods

We analyse how comprehensively value is assessed in nine countries in Europe. Our country selection includes the five biggest economies in Europe (France, Germany, Italy, Spain and the United Kingdom) and four other countries (Belgium, Poland, Norway and Sweden). Our country selection aimed to provide insight into how far a value-based approach to pricing is implemented in countries representing a range of geographies (North-western, Southern and Eastern Europe and the Nordics); healthcare system financing models (government or private healthcare insurance providers); and value assessment approaches. Regarding value assessment approaches, we sought to include countries practicing the following variety of approaches:

- **Therapeutic value (TV):** assessment of the health benefits offered by the medicine.
- **Therapeutic added value (TAV):** assessment of the additional health benefits offered by the medicine, compared to other medicines for the same indication.
- **Cost-effectiveness analysis (CEA):** assessment of the additional health benefits and costs of the medicine, relative to the health benefit and costs of an alternative treatment (the comparator, usually the best treatment currently available for the same indication).

Our results are primarily derived from a review of current guidelines and other official literature published by the bodies responsible for HTA and P&R policy in our sample countries, in addition to the Pharmaceutical Pricing and Reimbursement Information (PPRI) country profiles produced as part of a collaboration between the Austrian National Public Health Institute and World Health Organisation. For evidence of how a value-based approach to pricing in practice may diverge from official guidelines, we use information from the OECD publication 'Value in Pharmaceutical Pricing' (Paris and Belloni, 2013a), updated and supplemented with other relevant secondary literature identified through a targeted literature review. We restrict our scope to value assessment of innovative novel medicines, whether entirely new or for new indications.

We structure our analysis in section 2.3.1 on the coverage of value elements according to the value elements conceptualised in Paris and Belloni's (2013a) assessment of the implementation of a value-based approach to pricing in Europe. Each of these elements can be categorised as creating value within one of the three dimensions of value conceptualised in EFPIA's core value framework: value to the patient, value to the healthcare system, or value to society (EFPIA, 2019b). We also disaggregate the value element of 'health outcomes' to provide additional detail on this complex value element. These elements, and our definitions, are described below.

TABLE 1: VALUE ELEMENTS AND DEFINITIONS

Dimension of value		Definition
Value to patients	Health benefits	There are multiple components to the health benefits produced by medicines. There is some variation in how HTA bodies define and measure health benefits, but 'more commonalities than differences' (Paris and Belloni, 2013a). A simplified schematic to capture patient's health benefits includes: Clinical efficacy - refers to a medicine's effects on clinical outcomes, as observed in clinical trials. Safety of treatment and adverse events - the possible unintended negative effects on health that the medicine may cause in some patients. Health-related quality of life (HRQoL) - a summary measure of the effect of a medicine on a patient's QoL, as experienced through changes in life expectancy and morbidity.
	Improvements in the process of care	Effects which improve the patients' experience in receiving care, e.g., because of comfort of use, ease of administration, improved adherence (these may also be relevant to carers)
Value to healthcare systems	Costs of technology	Direct cost of purchasing the medicine being assessed
	Other direct medical costs	Other costs involved in the treatment pathway, including any costs associated with administering the treatment
	Indirect medical costs	The costs of treatments for unrelated medical conditions which occur because of the medicine's life extending properties
Value to society	Direct non-medical costs	Effects on patients' and caregivers' travel costs and leisure time
	Indirect non-medical costs	Effects on patients' and caregivers' productivity
	Health outcomes of carers	Effects on carers' mortality, morbidity and health-related quality of life (HRQoL)
	Disease severity	Effects on the equitable distribution of health, through treating severe diseases
	Disease rarity	Effects on the equitable distribution of health, through treating rare diseases
	Unmet need	Effects on the equitable distribution of health, through treating diseases for which no or inadequate treatments exist
	Equity	Overall effects on the equitable distribution of health. We include this despite the risk double-counting because a number of countries in our sample state that they value equity in general.
Innovation	Multiple dimensions including effects on the quality of future innovation due to scientific spillovers; effects on the delivery or organisation of care; and 'step changes' or major breakthroughs in treatment	

We structure our analysis of the use of a value-based approach to pricing, and other pricing approaches in section 2.3.2, according to the approaches identified in Paris and Belloni (Paris and Belloni, 2013a). For simplicity, we group these approaches into six categories, which are described in Table 2 below.

TABLE 2: PRICING APPROACHES AND PRICE CONTROL MEASURES

Approach/Policy	Definition and description with a value-based approach to pricing
Value assessment	The results of value assessment, e.g., through implementation of an explicit or explicit cost-effectiveness threshold (or cost-per-QALY) which technologies should meet, or through qualitative appraisal of the results of value assessment. A value-based approach to pricing is not only fully compatible with, but depends on, the results of value assessment being reflected in pricing.
Budget impact assessment	Consideration of budget impact. A value-based approach to pricing considers value to the healthcare system as well as patients and society – including through consideration of the costs of the technology. When this cost is accrued, and the resultant impact on healthcare resource use budgets, are important practical considerations, but determining prices with reference to budget impact assessment disrupts the alignment of value and price.
Therapeutic referencing	Therapeutic referencing places medicines to treat the same medical condition into groups or ‘clusters’ with a single common reimbursed price. It is, therefore, too blunt to be fully compatible with a value-based approach to pricing.
External referencing	External referencing is the practice of benchmarking the price of a product using the prices paid for the same product in other countries. These prices can diverge from the value the product offers in those countries (which may or may not be assessed), and products can offer different value in different countries; for both of these reasons, external referencing is not compatible with a value-based approach to pricing.
Measures to control spend on individual products	Measures to control spending on individual products include practices such as discounts or tendering of contracts which adjust prices reached through a value-based approach to pricing. Price-volume agreements, which offer price reductions when sales quantities increase; and expenditure caps, which set a maximum spend after which the product can be consumed at no cost; also distort the alignment between value and price.
Measures to control total pharmaceutical budget	Measures to control the total pharmaceutical budget, such as rebates and clawbacks (which return revenue accrued by innovators to healthcare systems), do not necessarily disrupt the relative alignment between value and price. However, to the extent that they decrease the effective or net prices achieved by companies below prices determined through value assessment, they are not compatible with a fully value-based approach to pricing.

To evaluate how far countries have implemented tools to manage uncertainty in section 2.3.3, we use three key indicators: the acceptance of surrogate outcomes in value assessment; the provision of methodological guidance to interpret surrogate outcomes in value assessment guidelines; and the use of outcomes-based MEAs in P&R. We present information on the two most common agreement designs, as identified by a 2019 OECD report (Wenzl and Chapman, 2019):

- **‘Coverage with evidence development’**, agreements whereby population-level reimbursement coverage is granted, conditional on further population evidence to reduce uncertainty and support future coverage decisions
- **‘Payment by results’**, agreements whereby (the level of) reimbursement is conditional for real-world performance, usually at the individual patient level.

2.3 Results

2.3.1 How comprehensively is value assessed by HTA bodies in Europe?

Figure 1 summarises our results regarding coverage of value elements in HTA bodies' guidelines, which are presented in more detail in Table 3 on the subsequent pages.

FIGURE 1: VALUE ELEMENTS RANKED IN ORDER OF HOW MANY COUNTRIES CONSIDER THEM IN VALUE ASSESSMENT

Considered in value assessment?	Yes	No
Health outcomes		
Cost of technology		
Other direct medical costs		
Treating severe diseases		
Direct non-medical costs		
Indirect non-medical costs		
Equity		
Health outcomes of carers		
Reducing unmet need		
Innovation		
Indirect medical costs		
Improvements in the process of care		
Treating rare diseases		

Key								
Belgium	France	Germany	Italy	Norway	Poland	Spain	Sweden	UK

From these results, we draw a number of conclusions:

- There are some value elements which all countries theoretically consider, although there may be variation in if they are considered in practice. All countries' HTA guidelines state that health outcomes of patients; costs of technology; and other effects on healthcare system resource use should be considered as part of value assessment. However, secondary literature suggests that healthcare resource use may not be consistently considered in value assessments in practice (Paris and Belloni, 2013a).
- All countries make some provision for capturing broader dimensions of value to society. Countries differ in whether value assessment considers economic value accrued to society beyond the healthcare system, but all countries' guidelines state that treating severe diseases should be considered in value assessment.
- Some value elements are rarely considered in value assessment. The least recognised value elements are innovation, which is only considered in France, Italy and the UK; the value of treating rare diseases, which is considered in the UK, Sweden and Norway; improvements to the process of care, which is only considered in France,

Germany and Belgium; and indirect medical costs, which is only considered by Sweden, France and Germany.

- **Some value elements are considered but only as part of additional scenarios.** Productivity, or 'indirect non-medical costs', are considered in value assessment in six countries, but only in additional scenarios which are provided alongside the 'reference case' or central assessment. It is challenging to determine how much weight is given to these additional scenarios in HTA body decision-making.
- **Some value elements are mentioned in guidelines but there is a lack of methodological guidance to facilitate this in practice.** Carers' health outcomes are potentially considered in five countries: France, Germany, Norway, Sweden and the UK. However, there is limited information on which methodologies and evidence should be employed to assess this value element. For example, the German HTA guidelines simply state that "Interventions can also have consequences for those indirectly affected, for example, relatives and carers. If appropriate, these consequences can also be considered within the framework of the Institute's reports" (IQWiG, 2020). In addition, the G-BA rules of procedure, which determine which aspects can legally be considered in decision-making around new medicines, state that health economic parameters beyond the patient-relevant "can be collected according to health economic standards" but gives no detail on if or how such evidence can be considered (Gemeinsamer Bundesausschuss, n.d.). In the UK, NICE's latest HTA guidelines allow for the inclusion of effects on carers' quality of life but stop short of providing a set of minimum evidence requirements to support their inclusion (NICE, 2022a).



TABLE 3: ELEMENTS OF VALUE CONSIDERED IN VALUE ASSESSMENT, ACCORDING TO COUNTRIES' HTA GUIDELINES

	Value to patients		Value to healthcare systems					Value to society						Source
	Health outcomes	Improvements in the process of care	Cost of technology	Other direct medical costs	Indirect medical costs	Direct non-medical costs	Indirect non-medical costs	Health outcomes of carers	Treating severe diseases	Treating rare diseases	Reducing unmet need	Equity	Innovation	
Norway	Clinical effectiveness; safety and adverse events; HRQoL		Included in CEA	Included in CEA		Included in CEA		Included in CEA if relevant	Considered through acceptance of (implicit) higher cost-effectiveness threshold	Considered through acceptance of (implicit) higher cost effectiveness threshold				(NoMA, 2018) (Norwegian Ministry of Health and Care Services, 2017)
Poland						Additional scenario	Additional scenario		Considered through acceptance of (implicit) higher cost-effectiveness threshold, based on provision in reimbursement Act.		May be considered qualitatively		(AOTMiT, 2009) (Badora et al., 2017)	
Sweden						Additional scenario	Included in CEA	Included in CEA if relevant	Considered through acceptance of (implicit) higher CE threshold	Considered through acceptance of (implicit) higher CE threshold	Considered qualitatively through principle of 'human value'		(SBU, 2020) (TLV, 2020) (Siverskog and Henriksson, 2021)	
Germany		(Considered if proven to affect health outcomes)				Reimbursable costs considered		Potential additional scenario	Changes in more severe outcomes are considered to offer greater benefit				(IQWiG, 2020; Gemeinsamer Bundesausschuss, 2011)	
Spain *						Additional scenario			Considered in assessment of TAV	Availability of other treatments considered in assessment of TAV	Effects on vulnerable subgroups of the population considered in TAV assessment		(Vogler, 2020b); (Paris and Belloni, 2013b)	

*Note: in Spain, the Spanish Medicines Agency (Agencia Española de Medicamentos y Productos Sanitarios [AEMPS], part of the Spanish Ministry of Health) has conducted value assessment of innovative medicines since 2013 (Epstein and Espín, 2020). There are no published guidelines for value assessment, and so we base our results on secondary literature and discussion with the Spanish trade association Farmaindustria

Key:	
	Considered in assessment of cost-effectiveness (CEA)/therapeutic added value (TAV)/therapeutic value (TV)
	Potentially considered in value assessment in an additional scenario (non-reference case analysis)
	For countries using cost-effectiveness: Considered in principle in overall value assessment, but qualitatively alongside results of cost-effectiveness analysis



	Value to patients		Value to healthcare systems				Value to society						Source				
	Health outcomes	Improvements in the process of care	Cost of technology	Other direct medical costs	Indirect medical costs	Direct non-medical costs	Indirect non-medical costs	Health outcomes of carers	Treating severe diseases	Treating rare diseases	Reducing unmet need	Equity		Innovation			
France		For TV, considered as part of assessment of public health benefit For TAV, considered if proven to affect health outcomes	Included in CEA	Included in CEA	Additional scenario	Included in CEA	Additional scenario	Included in CEA if relevant	'Seriousness of the disease' considered in assessment of TV and TAV		For TV, other therapies available and 'public health benefit' in terms of unmet need, considered For TAV, Level of 'medical need' considered		Assessment of TAV includes innovation criterion, defined in terms of novelty of action; unmet need; and efficacy	(HAS, 2020a); (HAS, 2020b)			
Italy						Additional scenario					Therapeutic added value in the treatment of severe diseases one factor in determining level of innovation		Unmet or 'therapeutic' need one factor in determining level of innovation		Medicines classified by level of innovation (fully/ conditionally/ non-) according to level of therapeutic need, TAV and quality of evidence available	(AIFA, 2018); (AIFA, 2020)	
Belgium		May be considered qualitatively						Additional scenario			May be considered qualitatively		May be considered qualitatively				(KCE, 2012)
UK	Clinical effectiveness; safety and adverse events; HRQoL									Included in CEA if Relevant	Considered through acceptance of higher CE threshold (weighting of up to 1.7)	Considered through acceptance of higher CE threshold (weighting up to 3 & threshold of £100,000 for ultra-rare)	(Partly reflected in severity definition)	May be considered qualitatively	Elements that cannot be captured in the ICER may be considered qualitatively	(NICE, 2022a)	

Key:	
	Considered in assessment of cost-effectiveness (CEA)/therapeutic added value (TAV)/therapeutic value (TV)
	Potentially considered in value assessment in an additional scenario (non-reference case analysis)
	For countries using cost-effectiveness: Considered in principle in overall value assessment, but qualitatively alongside results of cost-effectiveness analysis

2.3.2 How far is a value-based approach to pricing of innovative pharmaceuticals implemented in Europe?

Figure 2 below summarises our results, which are presented in more detail in Table 4 overleaf.

FIGURE 2: VALUE ELEMENTS RANKED IN ORDER OF HOW MANY COUNTRIES CONSIDER THEM IN VALUE ASSESSMENT

Pricing approach or mechanism used?	Yes	No
A value-based approach to pricing		
<i>Alternative pricing approaches</i>		
Measures to control spending on individual products		
External referencing		
Measures to control total pharmaceutical budget		
Budget impact considerations		
Therapeutic referencing		

Key								
Belgium	France	Germany	Italy	Norway	Poland	Spain	Sweden	UK

From these results, we can conclude that all countries make some provision to reflect the results of value assessment in their P&R decisions. There may be a clear, mechanistic link, as in the case of countries using explicit cost-effectiveness thresholds, or a more deliberative and/or qualitative approach may be used. However, all countries also make use of other pricing approaches or price control measures that disrupt the alignment between value and price. Seven countries use external referencing, which is not only inconsistent with the principles of a value-based approach to pricing but may also be associated with patient access delays (as discussed in Section 1). All countries employ price control measures, and seven employ further measures, such as clawbacks to control the total pharmaceutical budget. Measures to control spending on individual products and on the total pharmaceutical budget drive a wedge between price and value and weaken the incentives to invest in the innovation pipeline relative to society's valuation of innovation.

TABLE 4: FACTORS INFLUENCING REIMBURSEMENT AND PRICING DECISIONS

	Main criteria used to inform reimbursement decisions		Main pricing mechanism	Approaches used to inform pricing				Measures to control spend on individual medicines ⁴	Measures to control total pharmaceutical budget
	Decision	Rate		Value-based	Budget impact considerations	Therapeutic Referencing	External referencing		
Norway	Cost-effectiveness: explicit threshold for acceptable incremental cost-effectiveness ratio (ICER) (Weise, 2018)	Reimbursement of drugs at 100% if found cost-effective during HTA, and 61% otherwise (Weise, 2018)	For non-hospital products, regulation: maximum price set by Norwegian Medicines Agency (Weise, 2018). For Hospital products: Negotiation with reference to explicit cost- effectiveness threshold ⁹	Cost-effectiveness: if the ICER is not acceptable, subsequent price negotiation to reach threshold (Weise, 2018)	In general, reimbursement scheme (for non-hospital products), a budget cap on NOK 100 million annually exists. Medicines exceeding this cap are assessed by the Ministry of Health and, if necessary, Parliament (Weise, 2018).	For hospital products where specialist assessment groups exist. New methods allow for clustering of medicines which are considered therapeutically comparable. A positive reimbursement decision then depends on the offering a price which is equal to or lower than the comparable products (Sekretariatet for nye metoder, 2022).	For non-hospital products, "The key mechanism for setting maximum prices": mean of the three lowest market prices of the product in basket of 9 countries (Weise, 2018)	National level tendering (Vogler, Paris and Panteli, 2018)	-
Poland	Cost-effectiveness: explicit threshold for acceptable ICER (Jahnz-Rozyk et al., 2017) Budget impact may also be considered (Jahnz-Rozyk et al., 2017)	N/A: Inpatient medicines covered by public payer; reimbursement level of outpatient medicines determined by drug type (Jahnz-Rozyk et al., 2017)	Negotiation with reference to explicit cost-effectiveness threshold (Jahnz-Rozyk et al., 2017)	Cost-effectiveness: appraisal may recommend with condition to reduce cost to ICER threshold (Jahnz-Rozyk et al., 2017)	Budget impact may be considered (Jahnz-Rozyk et al., 2017)	Limit groups for therapeutically similar drugs used to set maximum price (Jahnz-Rozyk et al., 2017)	Lowest price from a basket of 31 countries used as reference in price setting (Jahnz-Rozyk et al., 2017)	Confidential discounts; price-volume agreements; rebates; utilisation caps (Jahnz-Rozyk K. et al., 2017; Vogler, Paris and Panteli, 2018)	Clawback if pharmaceutical spending exceeds 17% of National Health Fund expenses; 50% of overspend is paid back by companies (Lis, 2017)

⁴ We report price control measures for which there is evidence of recent use; the frequency with which these are used was beyond the scope of the desk research.

	Main criteria used to inform reimbursement decisions		Main pricing mechanism	Approaches used to inform pricing				Measures to control spend on individual medicines ⁵	Measures to control total pharmaceutical budget
	Decision	Rate		Value-based	Budget impact considerations	Therapeutic Referencing	External referencing		
Sweden	Cost-effectiveness: implicit threshold (Ponten, Ronnhelm and Skiold, 2017)	-	Negotiation (Ponten, Ronnhelm and Skiold, 2017)	Cost-effectiveness compared to implicit threshold (Ponten, Ronnhelm and Skiold, 2017)	-	-	-	Confidential discounts (regional); hospital-level tendering; price-volume agreements; rebates (regional) ⁶ (Carone, Schwierz and Xavier, 2012; Vogler, Paris and Panteli, 2018; Wallstrom, 2017)	-
Germany	N/A: all drugs reimbursed unless in category excluded from reimbursement (OECD, 2018b)	N/A	Negotiation (OECD, 2018b)	TAV justifies a premium compared to reference prices. Cost-effectiveness considered primarily when price negotiation/arbitration fail (IQWiG, 2020); although the GBA-s code of procedure (Gemeinsamer Bundesausschuss, n.d.) recommends that "appropriateness" of cost coverage with reference to cost-effectiveness should be considered.	Not legally mandated, although the GBA-s code of procedure recommends that "reasonableness of cost coverage" (IQWiG, 2020), which includes budget impact, should be considered (Gemeinsamer Bundesausschuss, n.d.)	For drugs with TAV, prices of comparable therapeutics considered; maximum statutory price set for drugs without TAV using reference price clusters (OECD, 2018b)	For drugs with TAV, prices paid in other European countries are considered in price negotiations (OECD, 2018b)	Confidential discounts; mandatory discounts (retail & outpatient sectors); national-level tendering; regional-level tendering. The draft Act for the Financial Stabilization of the Germany Statutory Health System also makes provision for use of price-volume agreements. (Espin et al., 2018; Ferrario and Kanavos, 2013; OECD, 2018a; Morgan, Daw and Thomson, 2013; Carone, Schwierz and Xavier, 2012)	Mandatory rebates on outpatient drugs. Currently 7% but expected to rise to 12% in 2023 (Eversana, 2022)

⁵ We report price control measures for which there is evidence of recent use; the frequency with which these are used was beyond the scope of the desk research.

⁶ Budgetary responsibility for new medicines in Sweden is at the regional level, hence measures to control product-specific spend are also regional (Prieto-Pinto et al., 2020)

	Main criteria used to inform reimbursement decisions		Main pricing mechanism	Criteria used to inform pricing				Measures to control spend on individual products	Measures to control total pharmaceutical budget
	Decision	Rate		Value assessment	Budget impact	Therapeutic Referencing	External referencing		
Italy	TV, TAV, cost-effectiveness; unmet need; level of innovation and budget impact considered; drugs with innovative status can be reimbursed through one fund with 1,110 million euros for innovative medicines in 2022 (1,200 in 2023 and 1,300 in 2024) (Vogler, 2021)	N/A	Negotiation primary policy, but regulation in place for reimbursable medicines (Vogler, 2021)	TV, TAV, cost-effectiveness; unmet need and level of innovation may be considered in price negotiation (Paris and Belloni, 2013b)	Budget impact is considered in price negotiations (Paris and Belloni, 2013b)	-	No specific external referencing policy, but prices paid in other European countries are included in value assessment submissions and may be considered in price negotiations (Vogler, 2021)	Confidential discounts; expenditure caps; price-volume agreements, MEA (Vogler, 2021; Ferrario and Kanavos, 2013; Carone, Schwierz and Xavier, 2012; Vogler, Paris and Panteli, 2018; Espin et al., 2018)	Clawback if pharmaceutical spending exceeds a fixed proportion of total health budget, in 2021 of 14.85% divided into 7% for retail and 7.85% in non-retail. 100% of overspend is paid back by companies in retail and 50% in non-retail. Innovative products (innovative drugs) not included as they are funded with a specific fund (Vogler, 2021)
Belgium	TV; price; clinical effectiveness taking into account unmet need and population health needs; cost-effectiveness and budget impact considered (KCE, 2012)	TV: reimbursement level varies from 100% to 20% depending on level of TV (DeSwaef and Antonissen, 2008)	Regulation: Ministry of Economic Affairs sets maximum price (subsequent negotiation on actual applied price possible during reimbursement) (DeSwaef and Antonissen, 2008)	TAV allows price premium (DeSwaef and Antonissen, 2008)	-	Used to set maximum price for drugs; for drugs with TAV, a price premium is granted (DeSwaef and Antonissen, 2008; Paris and Belloni, 2013b)	For drugs without added TV, external referencing used in combination with therapeutic referencing (DeSwaef and Antonissen, 2008)	Confidential discounts; expenditure caps; hospital-level tendering; national-level tendering; price-volume agreements (Carone, Schwierz and Xavier, 2012; DeSwaef and Antonissen, 2008; Ferrario and Kanavos, 2013, 2015; KCE, 2012; Neyt et al., 2020; Vogler, Paris and Panteli, 2018)	Clawback tax of up to 4% of total annual medicines budget, if budget is exceeded (Wyckmans, D'herde and Meskens, 2022)

	Main criteria used to inform reimbursement decisions		Main pricing mechanism	Criteria used to inform pricing				Measures to control spend on individual products	Measures to control total pharmaceutical budget
	Decision	Rate		Value assessment	Budget impact assessment	Therapeutic referencing	External referencing		
United Kingdom (England only)	Cost-effectiveness: explicit threshold for acceptable ICER (Anderson et al., 2022)	All medicines found to be cost-effective reimbursed, but 'optimised decision-making' allows for reimbursement only for cost-effective patient subgroups (Bulut, O'Neill and Cole, 2020)	Nationally-led negotiation processes make reference to explicit cost-effectiveness threshold (Paris and Belloni, 2013b)	Cost-effectiveness: if the ICER is not acceptable, subsequent price decreases to reach threshold (Paris and Belloni, 2013b)	Budget Impact Test leads to further negotiation for medicines expected to exceed budget impact of £20 million in any of first 3 years (NICE, 2018)	-	-	Confidential discounts; hospital- & national-level tendering. Price-volume agreements (Anderson et al., 2022; Carone, Schwierz and Xavier, 2012; Ferrario and Kanavos, 2013; Hawkes, 2019; Kullman, 2010; Morgan, Daw and Thomson, 2013)	Voluntary scheme (VPAS) caps growth in annual branded medicines budget to 2% annually until 2023, with rebate if cap exceeded (15% in 2022) (DHSC, 2022)
Spain	TAV; cost-effectiveness; budget impact; place of medicine in treatment pathway (Vogler, 2020b)	N/A: co-payments for non-hospital products, with level determined by individuals' income and other demographic characteristics (Vogler, 2020b)	Negotiation primary policy, but regulation in place for reimbursable medicines (Vogler, 2020b)	TV and cost-effectiveness considered in pricing decisions (Vogler, 2020b)	Budget impact considered in pricing decisions (Vogler, 2020b)	-	External referencing sometimes used, predominantly for new medicines; rule is to take minimum price in basket (Vogler, 2020b)	Confidential discounts; price-volume agreements; rebates (retail); expenditure caps (Carone, Schwierz and Xavier, 2012; Espin et al., 2018; Ferrario and Kanavos, 2013; Pinyol et al., 2018)	Mandatory discount of 7.5% for new medicines on all medicines sold to the national health service (4% for orphan medicines) (Vogler, 2020b)

	Main criteria used to inform reimbursement decisions		Main pricing mechanism	Criteria used to inform pricing				Measures to control spend on individual products	Measures to control total pharmaceutical budget
	Decision	Rate		Value assessment	Budget impact assessment	Therapeutic referencing	External referencing		
France	TV: all drugs offering some level of clinical benefit are listed (Vogler, 2020a)	TV: reimbursement level varies from 100% to 0% depending on level of TV (Vogler, 2020a)	Negotiation (Vogler, 2020a)	TAV sets parameters for price negotiation: only drugs offering moderate TAV or above can be priced higher than existing therapeutic alternatives; cost-effectiveness can inform price negotiations ⁵	Budget impact may be considered in price negotiation ⁵	Used to set maximum statutory price for drugs with less than moderate TAV ⁷ (Vogler, 2020a)	Used to set maximum statutory price for drugs with moderate TAV or above (Vogler, 2020a)	Hospital-level tendering; price volume agreements (Vogler, 2020a, p.202; Ferrario and Kanavos, 2013; Carone, Schwierz and Xavier, 2012)	Targets set for annual growth in medicines spend (1.08% since 2004) and pharmaceutical companies' total sales (0.5% in 2021); clawbacks from companies capped at 10% of total annual revenue (Rodwin M.A., 2021)

⁷ For outpatient care and expensive inpatient care

2.3.3 How able to facilitate access in the context of uncertainty?

Table 5 presents our results in relation to value assessment in the context of uncertainty. The guidelines of HTA bodies in all countries state that they are willing to consider surrogate endpoints, although only three include methodological advice on the statistical methods that should be used for the validation and assessment of acceptability of surrogate endpoints included in HTA submissions. All HTA bodies have also made use of innovative payment models to facilitate reimbursement of health technologies for which significant uncertainty exists at the point of value assessment.

TABLE 5: MEASURES FOR MANAGING UNCERTAINTY

	Surrogate endpoints considered? (Grigore et al., 2020)	Methodological advice provided? (Grigore et al., 2020)	Measures to manage uncertainty ⁸
Norway	Yes	No	Coverage with evidence development (Wenzl and Chapman, 2019) Payment by results
Poland	Yes	Yes	Payment by results (Vogler, Paris and Panteli, 2018)
Sweden	Yes	No	Coverage with evidence development (Ferrario and Kanavos, 2013, 2015) Payment by results (Wenzl and Chapman, 2019)
United Kingdom (England only)	Yes	Yes	Coverage with evidence development (Ferrario and Kanavos, 2013; Wenzl and Chapman, 2019) Payment by results (Ferrario and Kanavos, 2015)
France	Yes	No	Payment by results (Ferrario and Kanavos, 2013; Wenzl and Chapman, 2019)
Germany	Yes	Yes	<i>Not affecting coverage, but pricing subject to results may be agreed in negotiations with sickness funds/insurance providers</i> (Wenzl and Chapman, 2019)
Italy	Yes	No	Payment by or at results (Vogler, Paris and Panteli, 2018; Ferrario and Kanavos, 2013; Wenzl and Chapman, 2019)
Belgium	Yes	No	Coverage with evidence development (Wenzl and Chapman, 2019; Ferrario and Kanavos, 2015) Payment by results (Wenzl and Chapman, 2019)
Spain	Yes	No	Payment by results (Vogler, 2020b)

⁸ Where we have identified evidence of use of payment models to manage uncertainty, this is cited. We note that this evidence does not indicate the prevalence of the use of the payment models.

2.4 Discussion

Our results demonstrate that efforts to assess the value of novel medicines and to reflect this value in P&R decisions are widespread across Europe. Increasing the comprehensiveness of value assessment and reducing the use of alternative pricing approaches and price control measures would improve the alignment between price and value, and, therefore a country's ability to implement a value-based approach to pricing. However, a value-based approach to pricing also requires that absolute price levels provide sufficient incentives for pharmaceutical innovation to thrive. This requires governments to invest sufficiently in healthcare systems.

Although empirical evidence is limited, there are indications that the value societies place on health exceeds the level of investment. A recent review of explicit and implicit cost-effectiveness thresholds in Europe found that these are not evidence-based (Kourouklis et al., 2020). Moreover, there are indications that the thresholds used in other sectors are misaligned with those used in health. For example, the current recommendation of the Swedish Transport Administration is to use a value of statistical life of 40.5 SEK million (Elin et al., 2022), which corresponds to 2.4 million SEK per QALY or approximately €240,000 in 2017 prices, according to a presentation by the Swedish Institute of Health Economics (Persson, 2018). A review of reimbursement decisions in Sweden between 2005 and 2011 concluded that the lowest cost per QALY of declined reimbursements is Swedish kronor (SEK) 700,000 (€ 79,100), while the highest cost per QALY of approved reimbursements is SEK 1,220,000 (€135,600) (Nilsson, Svensson and Arnberg, 2014). In the UK, HM Treasury's Green Book provides an estimate of the WTP for a QALY of £70,000 in 2020/21 prices (updated from £60,000 in 2022 to account for inflation) (HM Treasury, 2022). The explicit cost-effectiveness threshold applied by NICE for most novel medicines continues to be £20,000-£30,000. To facilitate a truly value-based approach to pricing, more research is important to improve the understanding of the societal valuation of health and the value of investment in medicines and healthcare.

3. Future directions for value-based approaches to pricing

This section considers how stakeholders could collaborate to enhance the implementation of value-based approaches to pricing and achieve the ‘triple win’. It shares proposals for more extensive implementation of a value-based approach in Europe and complementary policies. Together, these will help to ensure that patients can access the most innovative medicines in a way which is sustainable for healthcare systems – while simultaneously securing a stream of investment into the development of healthcare innovations that best meet the needs of patients and society. Below we summarise our key recommendations:

3.1 Enhancing value assessment and recognition

Section 2 shows how countries in Europe are increasingly recognising ‘novel’ or ‘broader’ dimensions of value in value assessment. However, it also demonstrates that recognition of the value of novel medicines is piecemeal: there is significant variation between countries in terms of which dimensions of value are recognised in value assessment guidelines and how these are defined and measured, as well as heterogeneity within countries with regards to which elements of value are considered in value assessment in practice. Our case study on orphan medicines explores how value assessment of ‘novel’ or ‘broader’ dimension of value is evolving and where progress is still needed. These challenges also apply to many other types of health technologies, which generate value in underrecognized dimensions and so are consistently undervalued in value assessment – including vaccines (Sevilla et al., 2018; Bell, Neri and Steuten, 2021), antibiotics (Morel et al., 2020), and curative treatments (Institute for Clinical and Economic Review, 2019).

Case Study 3: evolution in NICE’s value assessment of orphan medicines

WHAT PROGRESS IS STILL NEEDED IN VALUE ASSESSMENT OF OMPs?

Despite the success of the EU’s OMP regulation in increasing availability of OMPs, there is still significant unmet need among sufferers of rare diseases. Patient access to existing OMPs remains highly variable in Europe. A recent study found that 93% are reimbursed in Germany, compared to 47% in England and 33% in Wales (Zamora et al., 2019). More comprehensive value assessment is therefore important to ensure patient access to treatments which, due to undervaluation, some healthcare systems are currently unwilling to fund.

HOW IS NICE’S APPROACH TO VALUE ASSESSMENT OF ORPHAN MEDICINES EVOLVING?

Defining value: NICE is continuing to iterate and refine its definitions of ‘novel’ and ‘broader’ dimensions of value, in line with new evidence on how society values these. The review found evidence – published since the introduction of the HST programme – that society does *not* value treatments for rare diseases more highly than other treatments due to them being rare in nature but places a higher value because of characteristics such as “the burden of illness, severity, the age of the population, and the desire to reduce health inequality” (NICE, 2020b). The magnitude of benefit was similarly found to be a “composite of several other potentially important decision-making factors” (NICE, 2020b). Whilst there is limited evidence on how far citizens of the United Kingdom value these other characteristics, the review found (mixed) evidence to support societal valuation of treatments for more severe diseases, and the updated NICE guidelines for non-HST novel medicines now includes a decision modifier (which adjusts the acceptable ICER) for severity (NICE, 2022b).

The revised guidelines for HSTs retain the provision for treatments for rare diseases to be considered cost-effective up to a threshold of £100,000 on the basis that this “implicitly capture[s]”

societal valuation of severity. Further evidence collection and complementary refinements to conceptual value assessment frameworks will undoubtedly be needed to increase the accuracy of how the value of OMPs – and other novel medicines – are assessed.

Measuring value: The NICE methods review also illustrates ongoing challenges in measuring ‘novel’ or ‘broader’ dimensions of value. Whilst NICE has recommended that effects on the QoL of caregivers should be included in value assessment since 2004 (NICE, 2004), they have provided no further guidance on how this should be done. Recognising the uncertainty this creates in appraisals, the methods review aspired to define a set of “minimum evidence standards” for caregiver QoL, but ultimately concluded that this was premature due to the need for stakeholder input into the “normative judgements” (or, why should it be included?) involved in assessing caregiver QoL and “technical issues” (or, how should it be included?) requiring additional academic research (NICE, 2020a). Developing robust and consistent measures of ‘novel’ and ‘broader’ dimensions of value is often challenging, as is aggregating these measures into an estimate of total value. However, progress is being made. For example, frameworks have been proposed for assessing the ‘broader’ or ‘novel’ value elements associated with gene therapies for ultra-rare diseases (Garrison et al., 2019). Further evidence collection and methodological developments in these fields will, therefore, also be important for facilitating the value assessment of OMPs and other novel medicines.

Recognising and rewarding value: Despite the challenges identified above in defining minimum evidence standards for caregivers’ QoL, in practice, NICE has frequently considered effects on caregivers’ burdens (either effects on QoL or costs) in value assessments of OMPs. 46% of the 81 submissions which had been made under the HST programme as of June 2020 included qualitative or quantitative evidence of effects on caregivers’ burdens, and this evidence was accepted by NICE in 84% of cases (Ofori et al., 2020). Indeed, evidence of caregivers’ burdens played a role in 89% of NICE’s decisions - indicated by a critique of its inclusion/exclusion or the highlighting of caregiver’s burden in decision-making frameworks (Ofori et al., 2020). This example illustrates how it is both feasible and important for value assessments to consider ‘novel’ or ‘broader’ value elements, even whilst methodological or evidentiary challenges may persist. Yet NICE continues to be unusual amongst value assessment bodies both for considering even some dimensions of the value which OMPs generate through ‘family spillovers’ and for providing explicit guidance that it is willing to do so (Berdud et al., 2020).

Recognition of other ‘broader’ or ‘novel’ dimensions of value which are particularly relevant to OMPs – for example, productivity, innovation, and severity – are similarly underrecognized. This means that resource allocation, and therefore patient access, for OMPs is sub-optimally low under current value assessments. Moreover, innovators’ incentives to invest in the R&D of new OMPs, and in demonstrating the full range of value which they generate, are also sub-optimally low.

As illustrated in our case study, challenges persist in defining and measuring value. There are also gaps in value assessment bodies’ recognition of value, even when this is relatively well-evidenced. It is vital that value assessment bodies retain high standards of rigour in their methodologies for assessing value and the evidence they are willing to accept. However, how far ‘novel’ or ‘broader’ dimensions of value are defined and measurable is endogenous to how far they are recognised. Innovators of novel medicines, who typically fund the evidence collection required to produce inputs for value assessment, will prioritise demonstrating value in the dimensions which are recognised in value assessment. Similarly, a value-based approach to pricing incentivizes innovators to invest in R&D of novel medicines which create maximum value – but only along these dimensions recognised in value assessment.

‘Family spillovers’ provides an illustration of the consequences for society: if these were more widely recognised, it is expected that greater incentives would exist to develop not only OMPs, but novel medicines for conditions such as Alzheimer’s, multiple sclerosis and schizophrenia that generate

enormous psychological and physical burdens for caregivers worldwide (Bauer et al., 2020; Park, Marcum and Garrison, 2022; Maguire and Maguire, 2020; Shamsaei, Cheraghi and Bashirian, 2015). The “value of hope” or “value of cures” is another example. There is growing evidence that patients prefer treatments with high variance in outcomes, and are willing to accept the risk of a worse response to a treatment in return for the hope of being cured (Berdud et al., 2020). This variation is characteristic of gene therapies, and incorporation of the “value of hope” into value assessment would help strengthen incentives for investment in gene therapies in line with their value to patients.

Recommendation 1: Ensure meaningful involvement of stakeholders in value assessment and recognition

Involvement of stakeholders including patients, clinicians and carers in value assessment and recognition processes is crucial for ensuring that all perspectives on value of novel medicines are captured and appropriately integrated into valuation and P&R decisions. Involvement of innovators at an early stage in the value assessment and recognition process is also important for facilitating discussion about which evidence should be collected during drug development, in order to facilitate a comprehensive assessment of value. Innovators and value assessment bodies should invest in earlier and more frequent pre-launch cooperation, for example, through increased development and engagement in joint scientific consultations.

Recommendation 2: Develop a shared and holistic definition of value

EFPIA proposes collaboration between patients, healthcare system and industry stakeholders to develop a joint, holistic definition of value at the country level. We also propose collaboration to define principles for how the value generated by innovation could be shared to balance static and dynamic efficiency. A joint definition of value should explicitly acknowledge that novel medicines generate many varied sources of value to patients, healthcare systems, and society. It could also acknowledge that developing the evidence base and methodologies needed to rigorously define and measure these is a challenging but important endeavour, best addressed through collaboration. Working towards standardised methods for measuring value dimensions, including health outcomes for patients, would improve comparability and interoperability of collected data.

There is heterogeneity in what different societies value, and it is important that value assessment bodies are able to reflect the values of the societies they represent in their value assessment frameworks. A holistic definition has the advantage of accommodating not only this societal-level heterogeneity but also the heterogeneity in which dimensions of value are most relevant to different novel medicines and therapy areas. This would begin to address the disadvantages that patients face in accessing novel medicines for which ‘novel’ or ‘broad’ dimensions of value are particularly relevant. It would also shift value assessment from reacting to the challenges posed by novel medicines to looking forwards towards realising the full potential of pharmaceutical innovation. Value assessment bodies would have the flexibility to adapt value assessment frameworks in line with the values of the societies they represent and ensure payers fund the medicines that benefit patients and society the most. Innovators would have the confidence to invest in R&D of the novel medicines, which they expect to generate the most value for society. Knowing that value assessment frameworks would be flexible enough to recognise and weight all elements of value included in the definition, innovators, patients and health system stakeholders could collaborate to develop the supporting evidence and methodologies that accurately measure the value of each new health technology allowing efficient resource allocation and R&D investment decisions.

Recommendation 3: Enhance collaboration and sharing expertise across member states

The EU Regulation 2021/2282 on health technology assessment (HTAR) (European Commission, 2022) came into effect in January 2022, providing an opportunity for collaboration. It applies as of January 2025 and is aimed at providing a transparent and inclusive framework for joint clinical

assessments and scientific consultations. It also aims to identify promising new health technologies and promote stakeholder cooperation. Expected effects of the HTAR are improved access to new health technologies in all member states, more efficient use of resources, improved quality of HTA across Europe and fewer duplicative efforts amongst innovators and national HTA bodies. The framework provides a context for developing a shared, flexible EU-level approach to value assessment and appraisal, which can also accommodate country, population, economic and health system level differences between Member states.

Recommendation 4: Recognise qualitative evidence of value through deliberative processes

Many value assessment bodies recognise value qualitatively when quantitative evidence is lacking. Consideration of qualitative evidence is an important enabler of more holistic value assessment, and can ensure that value assessment provides concrete incentives for innovators to make R&D decisions in line with a more holistic definition of value. In the longer term, a shared commitment to evidence collection should make quantitative assessment more feasible, but qualitative recognition of value provides an important first step. Countries should exchange good practices, with the involvement of all stakeholders, on how best to assess and include qualitative value dimensions in decision-making.

Deliberative processes for decision-making can be used to facilitate robust, transparent consideration of qualitative evidence. A deliberative process for value assessment, a form of structured decision-making, consists of procedures, activities, and events that support the informed and critical examination of an issue and the systematic consideration of heterogeneous arguments and evidence to guide a subsequent decision (Oortwijn et al., 2022). A recent HTAi and ISPOR Task Force report suggested good practices for designing and implementing deliberative processes for value assessment (Oortwijn et al., 2022), and NICE's latest value assessment guidelines recommend the use of structured decision-making to support deliberations in instances, for example, when the technology is "associated with significant benefits other than health" or "there are strong reasons to suggest that the health benefits of the technology have been inadequately captured" (NICE, 2022b).

3.2 Embracing a value-based approach to pricing

Section 2 shows that countries in Europe increasingly aspire to reflect value in their approaches to P&R. However, widespread implementation of other pricing approaches and price control measures act to disrupt the alignment between price and value, which is necessary to realise the benefits of a value-based approach to pricing. This section presents practical proposals to improve the alignment of price and value in markets for novel medicines in Europe for the benefit of patients, healthcare systems and innovators.

Recommendation 5: Fully embrace a value-based approach

Value-based approaches require that net prices are aligned with value, and the use of alternative pricing mechanisms disrupts this alignment. We recommend that countries should fully embrace a value-based approach by avoiding the use of alternative pricing approaches. As Section 1 outlines, therapeutic referencing, external referencing, and cost-plus pricing can all disrupt the alignment of price and value - and, therefore, the signals sent to innovators about where society wants R&D investment to be spent. They also all have other negative expected consequences for patients and healthcare systems, compared to a value-based approach to pricing.

Recommendation 6: Extend a value-based approach to the indication level

An indication-based approach to pricing, where prices for the same medicine vary according to the value generated in treating different indications, refines the signals sent to innovators by facilitating an even more specific alignment between price and value. It also generates incentives for manufacturers to invest in developing novel medicines for new indications for which they are effective and safe and, therefore, maximises the value a single product can provide to society – since these newer indications will not influence the pricing of the highest value indications, which are traditionally launched first. In addition to these dynamic efficiency benefits, it contributes to access and affordability *today* (Towse, Cole and Zamora, 2018). This is because an indication-based approach to pricing provides innovators with the incentives to launch for additional indications – increasing patient access to novel medicines and simultaneously contributing to competition by increasing the treatment options available for each indication.

Despite the attractiveness of an indication-based approach to pricing, recent literature reviews have found that many feasibility challenges to implementation remain in many countries in Europe (Towse, Cole and Zamora, 2018; Preckler and Espín, 2022; Flume et al., 2016). A systematic literature review published in 2022 identified data collection and supporting infrastructure, and the risk of high administrative burden and associated costs, as the main perceived barriers to ‘full’ implementation of an indication-based approach to pricing (Preckler and Espín, 2022). However, there are also examples of how countries have begun to operationalise some elements of an indication-based approach to pricing, for example, through blended pricing (reflecting a volume-weighted average price per indication) in France and Germany and indication-specific financial MEAs in Italy (Towse, Cole and Zamora, 2018; Flume et al., 2016). Progress towards an indication-based approach to pricing is possible, especially with further piloting and experimentation (Preckler and Espín, 2022), and can be expected to deliver a ‘win-win’ of both static and dynamic efficiency gains (Towse, Cole and Zamora, 2018).

3.3 Complementing value-based approaches with other tools

Recommendation 7: Use outcomes-based managed entry agreements to manage residual uncertainty

A value-based approach to pricing requires that prices are aligned with value, which implies that pragmatic approaches for efficient management of uncertainty are needed. This includes uncertainty about clinical efficacy; the duration of long-term effects; and financial uncertainty.

Uncertainty is a particular challenge for treatments for rare diseases (or OMPs) due to constraints around clinical trials in very small patient populations (Nicod et al., 2017), as well as for treatments where more than one product is used in combination, where value can hardly be accurately attributed to each component. Preventative medicines and medicines which generate a significant proportion of their benefit by allowing patients to avoid the use of other forms of healthcare, are examples of other types of novel medicines also subject to greater uncertainty. This is because many of their benefits may accrue over long time horizons or vary depending on the healthcare system in which they are implemented (Hogervorst et al., 2022).

Uncertainty is also a challenge for advanced therapy medicinal products (ATMPs) – a growing class of novel medicines which have the potential to treat and even cure rare diseases and cancers, and also hold major potential for reshaping the progression of diseases such as Alzheimer's disease, Parkinson's disease, and spinal muscular dystrophy (Hanna et al., 2016). ATMPs correct underlying genetic defects, offering the potential for transformational health gains – usually through a ‘one-off’ treatment (Jørgensen, Hanna and Kefalas, 2020). However, the long-term benefits associated with ATMPs cannot be observed in short-term clinical trials, and there may be considerable uncertainty

about the durability of their treatment effects and the resulting need for retreatment (Coyle et al., 2020; Drummond et al., 2019), as well as about the possibility of adverse events occurring after the trial period ends (Huygens et al., 2021). Finding mechanisms to facilitate reimbursement of novel medicines at value-based prices in the context of dealing with post-launch uncertainty is essential to ensure that patients can access breakthrough innovations and that further progress in the field continues to be an R&D priority for innovators.

Healthcare systems in Europe are increasingly experimenting with outcomes-based MEAs as a mechanism for facilitating value-based approaches to pricing in the context of uncertainty. This is illustrated by a review of reimbursement schemes for two recently launched ATMP cancer treatments, Kymriah® and Yescarta®, in France, Germany, Italy, Spain and the UK (England). The net price or payment is linked to individual patient-level outcomes such as survival and remission status through rebates (in Germany) and staged payments (in Italy and Spain) (Jørgensen, Hanna and Kefalas, 2020). In France and the UK, reimbursement has been granted temporarily, but with requirements for innovators to contribute to cohort-level data collection that will be used in future reassessments. Such schemes may risk that healthcare systems overpay for value during the initial evidence collection period, especially when dealing with high uncertainty. However, they involve lower costs and administrative burden than agreements requiring patient-level data collection and price adjustments based on patient data. In addition, these risks can be mitigated if schemes allow innovators to increase the prices of their products in line with new evidence on value.

There are additional challenges to implementing outcomes-based MEAs related to value assessment, including the selection of appropriate outcome measures or surrogate endpoints (Simoens, De Groote and Boersma, 2022). The recommendations in Section 3.2.1 above, in particular regarding increased dialogue between stakeholders about evidence collection for value assessment, can help to address these (Trowman, Powers and Ollendorf, 2021). It is also important that 'coverage with evidence collection' schemes are designed such that reassessment can result in higher or lower prices, in line with the value of the novel medicine. However, these examples illustrate that outcomes-based MEAs are feasible and can deliver patient access, at value-based prices, in the context of substantial uncertainty.

A second challenge which healthcare systems can face when implementing value-based approaches to pricing is managing the budget impact of high value novel medicines. ATMPs may be challenging because of the potentially transformative benefits they offer to patients, typically delivered through a one-off intervention but realised over a lifetime. Recent cures for Hepatitis C, which are high value and indicated for an (initially) substantial patient population have also created budget impact challenges for healthcare systems in Europe and worldwide (Danzon, 2018a; Iyengar et al., 2016). Instalment payments, which allow healthcare systems to spread the cost of treatment over time, have been proposed as a mechanism for managing this challenge and facilitating patient access (Danzon, 2018a). The staggered payment model of the outcomes-based MEAs agreed for Kymriah® and Yescarta® in Italy and Spain demonstrates that it is possible to defer (potential) payments into future financial years (Jørgensen, Hanna and Kefalas, 2020).

Recommendation 8: enhance data collection infrastructure to allow for iterative assessments of value post-launch

Holistic data collection and analysis across healthcare systems can enable more tailored assessments of value delivered in real-world settings (including for monitoring novel payment models and for managing uncertainty). Metrics for measuring different dimensions of value, including health outcomes for patients, should be standardised in order to increase comparability and reliability, building on the joint definitions of value developed by all stakeholders. Additionally, such visibility also allows manufacturers to better focus R&D efforts in areas where value for healthcare systems can be delivered better.

Recommendation 9: Fully committing to Equity Based Tiered Pricing

A value-based approach to pricing can help to ensure that the level of investment in pharmaceutical innovation – and quality and quantity of the innovation pipeline – reflect the value of innovation to society. However, it does not solve the challenge of how investment in innovation should be distributed between countries, given there are incentives at the country-level to underinvest. To improve patient access in the EU and globally, EFPIA has therefore proposed a conceptual framework for ‘Equity Based Tiered Pricing’ (EFPIA, 2022). This requires solidarity between countries– in addition to an overarching governance and infrastructure framework – to prevent the erosion of differential prices through external referencing and parallel trade. Price confidentiality must also be maintained for the same reason. Whilst this may be challenging, it also means that the EU is uniquely well-placed to implement an important first step towards improving patient access and healthcare system affordability worldwide through differential value-based prices.

Recommendation 10: Promote competition

A value-based approach to pricing works in synergy with a competitive market for medicines, to deliver healthcare system sustainability. Indeed, value-based pricing itself promotes product competition. It increases the number of innovations which are expected in the therapeutic areas prioritised by society and, since rewards for innovations are in-line with the improvements they offer on existing alternatives (society will only pay for more value), innovators are also incentivized to develop substantial improvements. These effects are strengthened with indication-based value-based approaches to pricing, which increase the precision of the alignment between price and value and ensure that innovators are incentivized to launch for additional indications - thus increasing the chances of having more than one option for the treatment of a single indication.

There are additional complementary tools available to policymakers for strengthening competition. Innovation in therapeutic areas of high unmet need, which, by definition, experience limited competition, has historically been challenging, including in Alzheimer’s, multiple sclerosis, and osteoporosis. To mitigate the high risk of investing in R&D in such areas – which often requires highly innovative scientific approaches – and thereby promote competition, streamlining regulatory pathways has been shown to be effective. One example is the EMA’s PRiority MEDicines (PRIME) initiative, which seeks to support the development of medicines targeting unmet needs through measures such as accelerated assessment and early dialogue on clinical trial design, as well as extended exclusivity periods. Early indications suggest that PRIME has been successful in increasing competition in areas of unmet need: in the first five years of PRIME, 95 medicines were accepted into the scheme, including some targeting the same indications (European Medicines Agency, 2021). There is also evidence that the EMA’s OMP Regulation (which incentivizes investment in OMPs through a combination of additional market exclusivity and protocol assistance) is beginning to increase competition, despite the small market sizes associated with OMPs. Between 2012 and 2018, most authorised OMPs have been for indications for which there is at least one other treatment available, with the share increasing from 21% in 2012 to 70% in 2018 (Berdud et al., 2020).

Conclusion

A value-based approach to pricing will help to deliver a sustainable stream of innovation, delivering the 'triple win', and so benefits patients, healthcare systems, and payers. Whilst many countries in Europe recognise the potential of a value-based approach, and experiment with its implementation, there is significant heterogeneity in how far this has been done and to what extent other pricing approaches act to disrupt the alignment of value and price. There are many opportunities to improve how a value-based pricing approach is implemented for the benefit of all stakeholders, and this is what we seek to encourage through our recommendations.

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About us

Founded in 1962 by the Association of the British Pharmaceutical Society, the Office of Health Economics (OHE) is not only the world's oldest health economics research group, but also one of the most prestigious and influential.

OHE provides market-leading insights and in-depth analyses into health economics & health policy. Our pioneering work informs health care and pharmaceutical decision-making across the globe, enabling clients to think differently and to find alternative solutions to the industry's most complex problems.

Our mission is to guide and inform the healthcare industry through today's era of unprecedented change and evolution. We are dedicated to helping policy makers and the pharmaceutical industry make better decisions that ultimately benefit patients, the industry and society as a whole.

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Areas of expertise

- Evaluation of health policy
- The economics of health care systems
- Health technology assessment (HTA) methodology and approaches
- HTA's impact on decision making, health care spending and the delivery of care
- Pricing and reimbursement for biologics and pharmaceuticals, including value-based pricing, risk sharing and biosimilars market competition
- The costs of treating, or failing to treat, specific diseases and conditions
- Drivers of, and incentives for, the uptake of pharmaceuticals and prescription medicines
- Competition and incentives for improving the quality and efficiency of health care
- Incentives, disincentives, regulation and the costs of R&D for pharmaceuticals and innovation in medicine
- Capturing preferences using patient-reported outcomes measures (PROMs) and time trade-off (TTO) methodology
- Roles of the private and charity sectors in health care and research
- Health and health care statistics