

The root causes of unavailability of innovative medicines and delay in access: Shortening the wait

Executive Summary¹

The unprecedented speed of innovation exhibited over the last five years and the promise of the industry pipeline² provide an important opportunity to improve outcomes for patients. There is common agreement that the value of innovation is realised only when patients benefit from advances in treatment. However, a significant number of medicines are not available across all European Union (EU) markets.³

EFPIA has for many years looked at the length of time it takes for medicines to be made available. As illustrated by the most recent data in the Patient W.A.I.T. Indicator Survey in 2023, the average time to reimbursement for innovative treatments across EU and European Economic Area countries has reached 531 days, ranging from 126 days in Germany to 990 days in Turkey.⁴ There are patient access inequities within Europe, with significant differences across countries in the number of products available at any given time and that the time taken prior to national reimbursement also varies significantly from one country to another. The industry shares concern about these delays and recognise that delays and the unavailability of medicines harm patients. These concerns are important context for the debate regarding the impact of the EU's General Pharmaceutical Legislation and whether it will improve access to medicines for patients in the EU.

Over the past four years, EFPIA has documented the root causes of access inequality and found 10 interrelated factors that explain unavailability and delay (defined as length of time from European marketing authorisation to availability at the member state level) with regard to innovative medicines, building on the W.A.I.T. analysis.⁵ These factors are rooted in medicines access systems and processes in the EU member states and the corresponding impact on commercial decision-making. They include a slow regulatory process, late initiation of market access assessment, duplicative evidence requirements, reimbursement delays, and local formulary decisions. Because the root causes are multifactorial, they can be solved only by stakeholders working together.

¹ Terminology: This paper has adopted the terminology used in the updated W.A.I.T. analysis. Definitions are in the glossary.

² IQVIA (2024) Global Trends in R&D 2024. Available at: <https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2024-activity-productivity-and-enablers> [accessed April 2024]

³ This paper focuses primarily on root causes of delay with respect to products approved centrally by the EMA. There are non-centrally approved medicines to which many of these root causes would also apply.

⁴ The Patient W.A.I.T. Indicator 2023 Survey. Note: No dates were submitted in total for Malta, so it is excluded from the range and average calculation.

⁵ <https://www.efpia.eu/publications/downloads/efpia/the-root-causes-of-unavailability-and-delay-to-innovative-medicines/>

Table 1: The root causes of delays and unavailability

Category	Potential root causes
The time before marketing authorisation	<ol style="list-style-type: none"> 1. The speed of the regulatory process 2. Accessibility of medicines before marketing authorisation
The price and reimbursement process	<ol style="list-style-type: none"> 3. Initiation of the process 4. The speed of national timelines and adherence
The value assessment process	<ol style="list-style-type: none"> 5. Misalignment on evidence requirements 6. Misalignment on value and price 7. The value assigned to product differentiation and choice
Health system constraints and resources	<ol style="list-style-type: none"> 8. Insufficient budget to implement decisions 9. Diagnosis, supporting infrastructure, and relevance to patients
The subnational approval process	<ol style="list-style-type: none"> 10. Multilayer decision-making process

The industry considers that the root causes of unavailability and delay could be addressed through collaborative work with member states, the European Commission, and other stakeholders on proposals to improve availability and reduce delays. This work must occur from the beginning of the process, including proposals to speed up the regulatory process to deliver safe, high-quality diagnostics, vaccines, and treatments to patients as fast as possible. The industry welcomes the European Parliament's commitment to developing a future-proof regulatory framework that is reflected in its recently adopted position on proposed reforms to EU pharmaceutical legislation. The industry also supports the pragmatic decision by Members of the European Parliament to not link regulatory data protection (RDP) to medicine availability.

Finding workable solutions to improve patient access to medicines will require multi-stakeholder collaboration and consideration of the multifactorial nature of root causes of unavailability and delay. EFPIA and its members have worked on a series of specific proposals to improve patient access to innovative medicines and reduce inequalities across Europe. The following are some of these proposals:

- **A commitment from the industry to file pricing and reimbursement (P&R) applications in all EU countries no later than two years after EU market authorisation, provided that local systems allow it.** This commitment reflects the joint ambition of industry and society to make innovation for unmet health needs available to patients and health systems across Europe as soon as possible.
- **The creation of a portal where marketing authorisation holders (MAHs) can provide timely information regarding the timing and processing of P&R applications in the 30 European countries.** Such information includes the reasons for delay in a P&R decision or the MAH having not filed in a particular

market. The portal is now in its second year of operation, and EFPIA has published two reports documenting the novel information collected in the portal and its relevance to the debate on medicine availability.⁶

- **A conceptual framework for equity-based tiered pricing (EBTP)** to ensure that ability to pay across countries is considered in the prices of innovative medicines, anchored in a principle of solidarity between countries, to reduce unavailability of new medicines and access delays.
- **Novel payment and pricing models** that, when used appropriately and tailored to the situation, can accelerate patient access, allowing payers to manage clinical uncertainty, budget impact, and sustainability of the healthcare system, while providing sufficient incentives for innovation.^{7,8}
- Contributions to the achievement of an **efficient system of European assessments of relative efficacy at time of launch** in the context of the implementation of the Health Technology Assessment (HTA) Regulation.

The present report is the fifth edition of the root cause analysis first released in June 2020, which was used as a basis for discussion with several EU and national policymakers and stakeholders. The present report takes stock of these discussions, updates the data and evidence, and further articulates how policy proposals can address some identified hurdles in a collaborative and sustainable way.

1.1. Background and approach

The unprecedented speed of innovation exhibited over the last decade and the promise of the industry pipeline provide an important opportunity to improve outcomes for patients. Innovative medicines have already significantly extended survival by delivering treatments to patients with chronic diseases and those with previously untreatable cancers, treating genetic conditions for which there were no medicines, and eliminating some infectious diseases.

There is common agreement that the value of innovation is realised only when patients benefit from advances in treatment. Everyone involved in healthcare—from patients to service providers, researchers to clinicians, pharmaceutical companies to payers—wants to see patients across Europe get access to new treatment options.⁹

The importance of addressing unavailability and delays was highlighted in the European Commission's proposal for reform of the General Pharmaceutical Legislation in Europe.¹⁰ The subsequent debate in the European Parliament has reflected this (see Box 1).

6 CRA, EFPIA (2023) European Access Hurdles Portal: initial results. Available at: <https://www.efpia.eu/media/677291/european-access-hurdles-portal-efpia-cra-report-200423-final.pdf> [accessed April 2024]

7 <https://efpia.eu/media/554543/novel-pricing-and-payment-models-new-solutions-to-improve-patient-access-300630.pdf>

8 <https://www.efpia.eu/media/602581/principles-on-the-transparency-of-evidencefrom-novel-pricing-and-payment-models.pdf>

9 <https://www.efpia.eu/news-events/the-efpia-view/blog-articles/how-long-should-you-wait-for-a-new-medicine-europe-s-post-code-lottery/>

10 European Commission (2023) Reform of the EU pharmaceutical legislation. Available at: https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/reform-eu-pharmaceutical-legislation_en [accessed April 2024]

Box 1: Discussion of root causes in the European Parliament's position on the European Commission's proposed reforms to EU pharmaceutical legislation

“ . . . these medicinal products do not always reach the patient and patients in the Union still have different levels of access to medicinal products. Patient access to medicinal products depends on many factors. Marketing authorisation holders are not obliged to market a medicinal product in all Member States; they may decide not to market their medicinal products in, or withdraw them from, one or more Member States often due to commercial reasons. National pricing and reimbursement policies, the size of the population, the organisation of health systems and national administrative procedures are other factors influencing market launch and patient access. In addition, a complex regulatory environment and associated administrative burden can prevent SMEs, research institutes and academic institutions from developing promising innovative treatments and from applying for conditional market authorisation.”

Source: European Parliament, European Parliament legislative resolution of 10 April 2024¹¹

In April 2023, the European Commission set out a proposal for a revision of the EU Pharmaceutical Legislation with a stated aim of ensuring access to medicines for all patients in the EU that links the length of the RDP baseline to the launch and supply of medicines in all EU-27 markets within two years following the grant of the EU marketing authorisation. While there is still some way to go until the legislation is finalised and approved, the European Parliament amended the Commission proposal in April 2024 by removing the link between RDP length and launch in all EU-27 markets and by including instead an obligation for pharmaceutical companies to submit an application for P&R in those member states that have requested it. For the reasons explored in this paper, primarily that the root causes of unavailability and delay are multifactorial (many of which extend beyond the control of MAHs and vary significantly across member states), there are good reasons to believe the Commission proposal may be unworkable in practice.

The industry shares the concern about unavailability and delay, recognises that delays and the unavailability of medicines harm patients, and agrees that there is a need to act urgently to address these long-standing issues. The purpose of this paper is to describe the factors that could explain unavailability and delay for patients across the EU and the degree to which they are supported by the most recently available data. On the basis of a common understanding, and focusing on the needs of patients, collaborative solutions can be found that address the issues raised in the report.

1.2. What do we mean by availability and delay?

In the European Union, once a new treatment has gone through a process of ten years of research and development, on average, three further milestones must be reached before patients have access to it (see Figure 1)**Error! Reference source not found.:**

- A European marketing authorisation confirming the quality, safety, and efficacy of the therapy must be granted.

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European Parliament legislative resolution of 10 April 2024 on the proposal for a directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC (COM(2023)0192 – C9-0143/2023 – 2023/0132(COD))

- National authorities must secure national (and regional) reimbursement of the therapy under an insurance or reimbursement scheme to secure the adequate provision of medicines to all patients. In some cases products are available without reimbursement on the private market, but this does not ensure wide access to the patient population.
- Once reimbursed, innovations need to reach the people they are intended for and should be used in accordance with their labels, the latest scientific insights, and relevant treatment guidelines (post-reimbursement access).

This paper focuses on availability and delays, so we focus on the first two milestones.

Figure 1: Milestones that must be reached to bring innovative therapies to patients

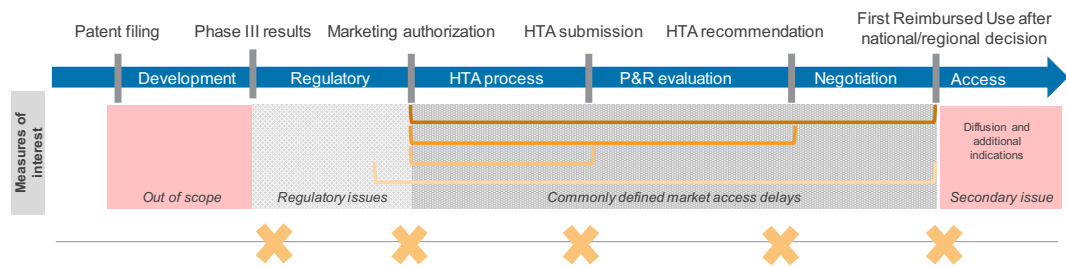


Source: EFPIA 2020

It is important to distinguish between several time points (Figure 2):

- The length of time between application for and the granting of marketing authorisation
- The length of time from market authorisation to application for P&R
- The length of time from application for P&R to a decision on value assessment
- The length of time from a decision on value assessment to a reimbursement decision

Figure 2: Types of delay in the availability of medicines

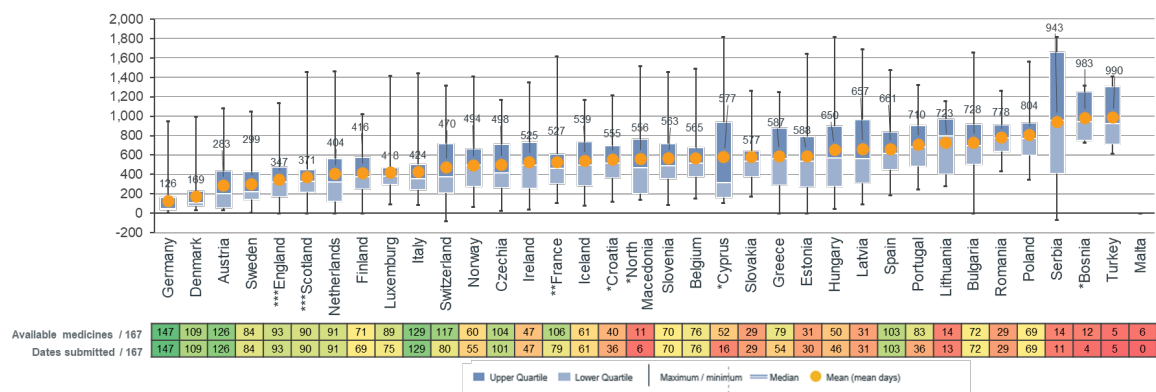


Source: EFPIA

1.3. What is the evidence on unavailability and delays?

EFPIA for many years has looked at the length of time it takes for medicines to be reimbursed. As illustrated by the most recent data in the Patient W.A.I.T. indicator 2023 survey (in Figure 3 below), the average time to reimbursement for innovative treatments across the EU and European Economic Area countries is 531 days, ranging from 126 days in Germany, to as long as 990 days in Turkey.

Figure 3: Mean time to availability in days (2019–2022)¹²



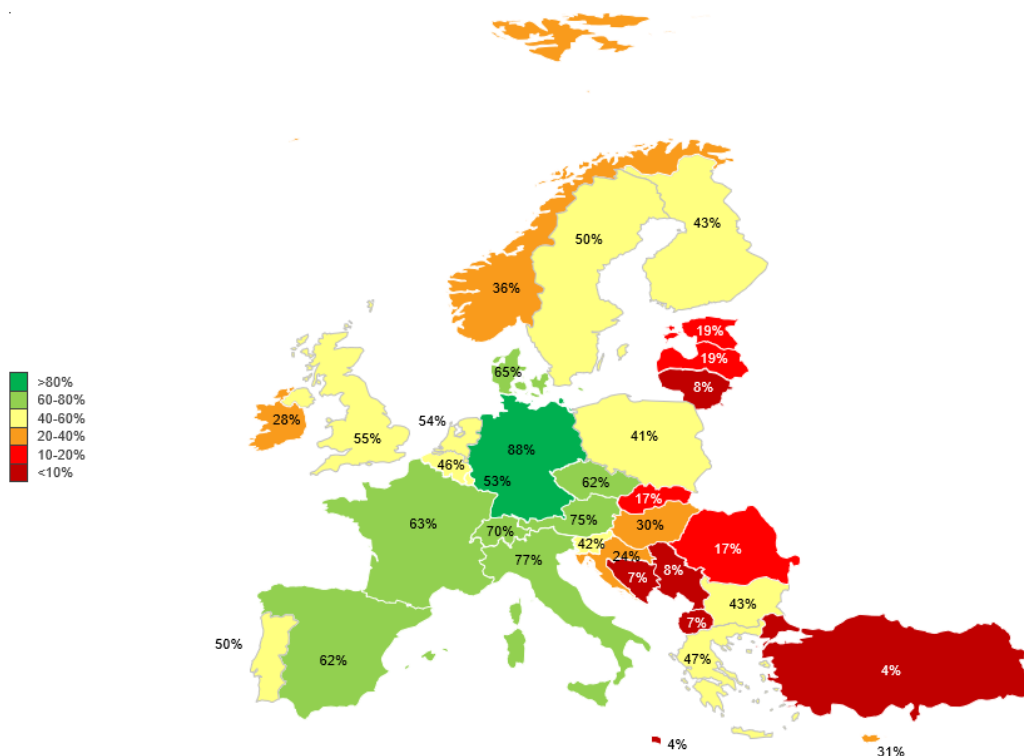
Source: The Patient W.A.I.T. Indicator 2023 Survey

Patients in certain European countries can wait more than 800 days longer than patients in other countries to get access to the same medicine. Some common patterns are evident: typically, patients in Northern and Western Europe get access to new treatments between 100 and 400 days after market authorisation has been granted, whereas patients in Southern and Eastern Europe wait between 500 and 1000 days. This means that at any time, availability of medicines varies dramatically across Europe (as shown in Figure 4 below).

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Malta is not included, as no dates were submitted.

Figure 4: Comparing availability across European countries (average % availability)



Source: *The Patient W.A.I.T. Indicator 2023 Survey.*

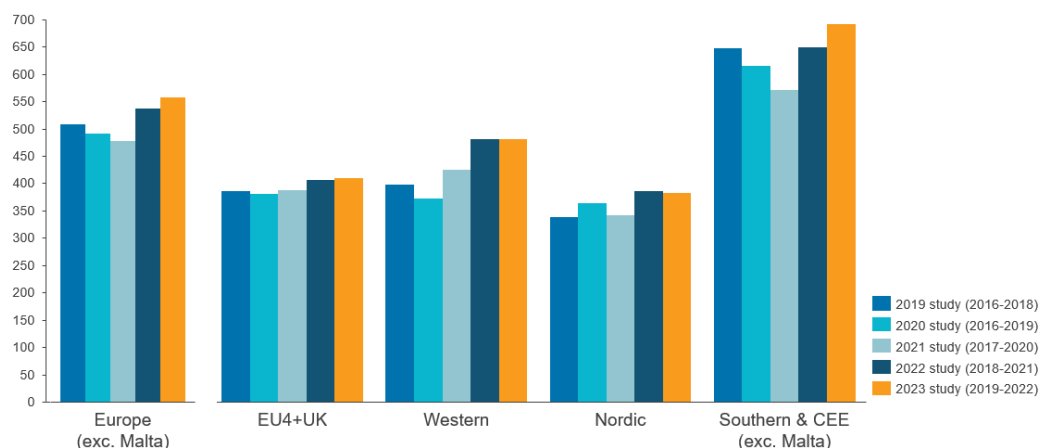
Variation in both time until availability and rate of availability has become more evident as data from more countries have been incorporated into this analysis, now in its fifth year. When this analysis was first published in 2020, time to availability ranged from 127 days in Germany to 823 days in Poland (a difference of 696 days).¹³ Since then, some countries have improved their time until availability, while others have worsened theirs; the overall inequity between countries has persisted. Now, the gap in time to patient access for innovative medicines has increased to 864 days between the fastest (Germany) and slowest (Turkey) countries in Europe.

There is also evidence to suggest that, across Europe, delays in availability of innovative medicines are gradually lengthening over time (see Figure 5Error! Reference source not found.). This is most obvious in Western European countries, but it is also the case in the EU4+UK and in the Nordics. Central and Eastern European (CEE) and Southern European countries, although experiencing the longest time until availability on average, have not experienced as significant an increase in delays over time.¹⁴

13 EFPIA & CRA (2020) “The root cause of unavailability and delay to innovative medicines” Available at: <https://www.efpia.eu/media/554527/root-causes-unavailability-delay-cra-final-300620.pdf> [accessed April 2024]

14 The countries were grouped by geography: **EU4+UK**: England, France, Germany, Italy, Scotland, Spain; **Western**: Austria, Belgium, Ireland, Luxembourg, Netherlands, Portugal; **Nordic**: Denmark, Finland, Iceland, Norway, Sweden; **Southern and Central and Eastern European (CEE)**: Bosnia, Bulgaria, Croatia, Cyprus, Czechia, Estonia, Greece, Hungary, Latvia, Lithuania, Malta, North Macedonia, Poland, Romania, Serbia, Slovakia, Slovenia, Turkey.

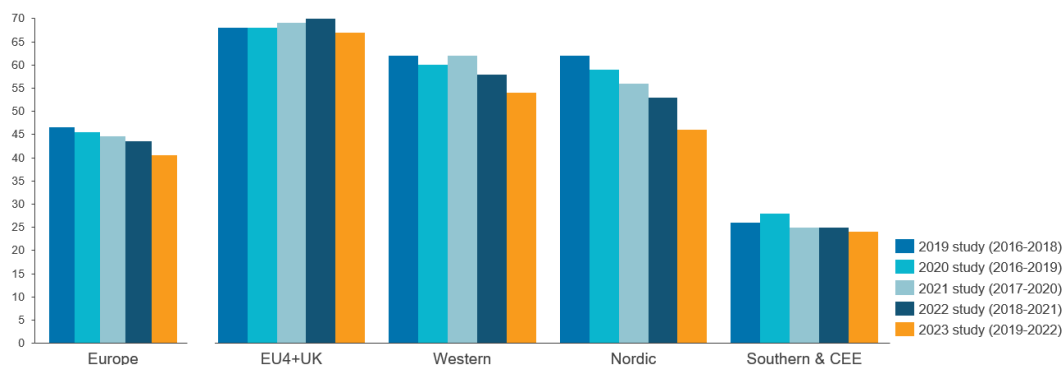
Figure 5: Comparison of delay over time (mean delays in days), by region¹⁵



Source: *The Patient W.A.I.T. Indicator 2023 Survey*. Note: Malta is excluded because data on time to availability were captured only in the 2022 study.

We can also look at how the availability of innovative medicines is changing over time across Europe (Figure 6). The evidence here also suggests a negative trend, with a decrease in availability for innovative medicines across the EU27 countries. This decline is most evidence in Western and Nordic countries. Although the rate of availability of innovative medicines is still lowest in Southern and CEE countries, rates there have changed only minimally over time.

Figure 6: Comparison of rate of availability over time (mean availability in percentage), by region

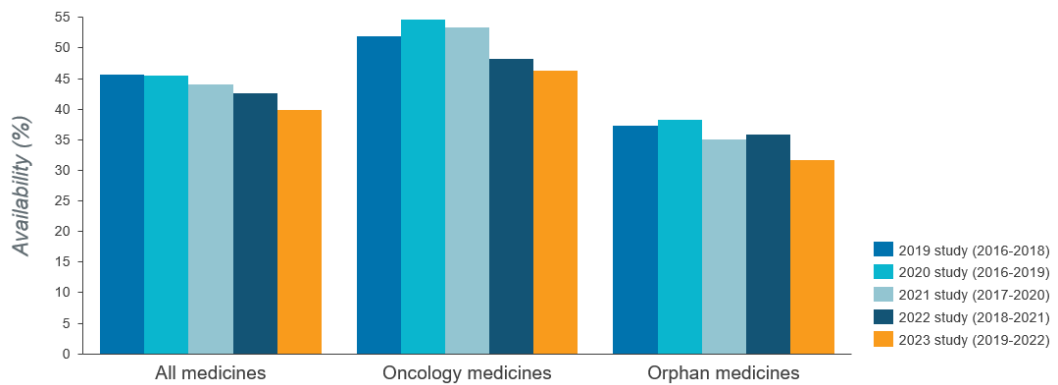


Source: *The Patient W.A.I.T. Indicator 2023 Survey*

Also observable are differences over time in access to different types of medicines (see Figure 7). The availability of oncology medicines, although remaining higher than for all medicines, has decreased over time. For orphan medicines, the rate of availability remains consistently lower and has fallen.

¹⁵ The European average was calculated using all 36 countries included in the W.A.I.T. data except Malta. These countries are then grouped by region to generate the region-specific evidence.

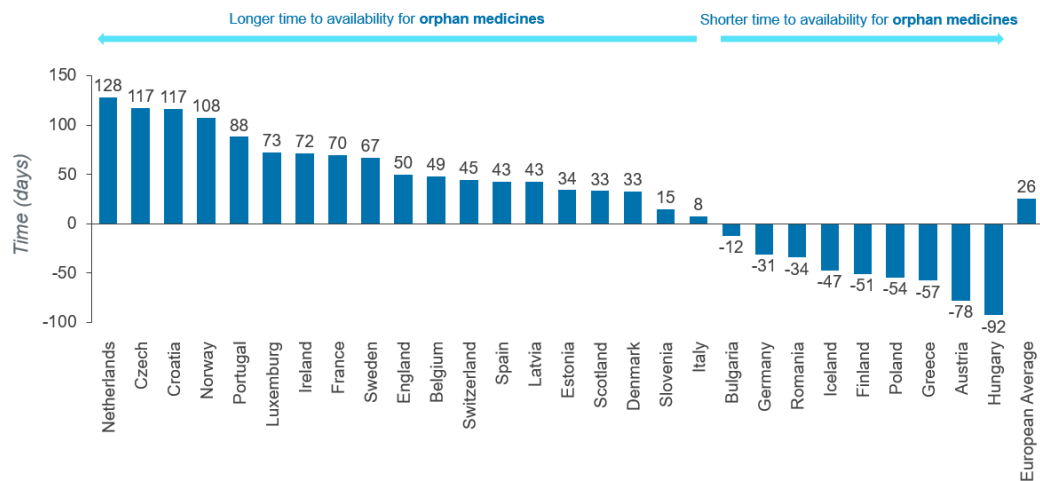
Figure 7: A comparison of availability across different medicine types, over time, in Europe



Source: *The Patient W.A.I.T. Indicator 2023 Survey*

Availability of orphan medicines continues to vary considerably across Europe, with longer delays and lower availability observed in CEE and Southern European countries. As shown in Figure 8, there tend to be major differences in access for orphan medicines compared to for all medicines, with faster time until availability for all medicines not necessarily aligning with faster time until availability for orphan medicines, perhaps reflecting the impact of designated access pathways for orphan medicines in certain countries.

Figure 8: Difference in the mean time to availability for all medicines vs. orphan medicines (2019–2022)



Source: *The Patient W.A.I.T. Indicator 2023 Survey*; based on local times to availability. Note: Positive values mean orphan drugs are slower than all medicines by the indicated number of days.

The observed variation in the length of delay and availability of types of innovative medicines, even within a single subregion of Europe, is consistent with findings in the literature. A recent academic study investigated access to innovative oncology medicines in four CEE countries: Czechia, Hungary, Poland, and Slovakia. The share of reimbursed

oncology medicines ranged from 19% in Slovakia to 64% in Czechia, while the median delay in availability ranged from 27 months in Poland to 37 months in Hungary.¹⁶

Significant variation also exists between individual medicines of the same type. Evidence suggests that, even within one country, patients can get access to some medicines almost immediately and wait years for others. For example, in Sweden, the shortest delay to oncology medicines was 8 days and the longest 838 days; in Scotland, the variance was 145 days to 1,453 days; in Spain, 254 days to 1,473 days.¹⁷

Although it is not possible to look at every therapeutic area using the W.A.I.T. data, additional studies indicate that long delays and variances across countries can also be observed in other therapy areas.¹⁸

1.4. What factors could explain unavailability and delay?

The causes of delays and unavailability have been debated for many years. Policymakers and nongovernmental organisations (NGOs) have often pointed out that industry uses approaches such as launch sequencing to determine the speed at which products get to market, and it appears to be a commercial decision. The industry has often argued that the long, complex practice of applying for reimbursement delays access to medicines. In reality, many interconnected factors could explain unavailability, and it is not possible to untangle their impacts with perfect precision. For example:

- In some markets, even if a product is reimbursed and available, it is not in practice used in the market (see Section 1.6). It is unsurprising that other manufacturers might choose to avoid the cost of applying for reimbursement.
- Other markets require that a product already be reimbursed in a series of comparable countries (see Section 1.5.2).¹⁹ Application for reimbursement is delayed until access in the other markets is achieved.

In other words, the environment affects commercial decisions. This paper seeks to tease out these factors. EFPIA has identified 10 factors from five perspectives: the time before market authorisation; the pricing and reimbursement process; value assessment criteria; health system constraints and resources; and delay from national to regional approval (Table 2).

¹⁶ Hofmarcher, T., Szilagyi, P., et al. (2023) Access to novel cancer medicines in four countries in Central and Eastern Europe in relation to clinical benefit. *ESMO Open* 8(4): 101593

¹⁷ The Patient W.A.I.T. Indicator 2023 Survey

¹⁸ For example, in diabetes we see that some therapeutic classes have experienced particular challenges: SGLT-2 inhibitors gained reimbursement in France only in 2020, 8 years after EMA approval; in Poland, it took 12 years for long-acting insulins to be reimbursed after their first EMA approval. EFPIA and PwC analysis (2023) [unpublished]

¹⁹ Greece: article 22 of Law 4633/2019: medicines with patent protection are subject to HTA in Greece only if they are reimbursed in five other countries with an HTA process from the following list: Austria, Belgium, France, Germany, Denmark, Spain, Netherlands, Italy, Portugal, Sweden, and Finland.

Table 2: The root causes of unavailability and delay

Category	Potential root causes
The time before marketing authorisation	<ol style="list-style-type: none"> 1. The speed of the regulatory process 2. Accessibility of medicines before marketing authorisation
The price and reimbursement process	<ol style="list-style-type: none"> 3. Initiation of the process 4. The speed of national timelines and adherence
The value assessment process	<ol style="list-style-type: none"> 5. Misalignment on evidence requirements 6. Misalignment on value and price 7. The value assigned to product differentiation and choice
Health system constraints and resources	<ol style="list-style-type: none"> 8. Insufficient budget to implement decisions 9. Diagnosis, supporting infrastructure, and relevance to patients
The subnational approval process	<ol style="list-style-type: none"> 10. Multilayer decision-making process

Source: EFPIA

We now turn to the evidence of what causes unavailability. As set out in the OECD analysis, this needs to be considered carefully. All stakeholders should jointly work to improve availability but should not expect availability to be 100%: “Broad access to all . . . medicines is often assumed to be ideal, but is not essential. For example, if several medicines are potentially available for a given indication, procurement methods may result in only some of them being available, without disadvantaging patients.”²⁰

1.5. Root causes of unavailability and delay

1.5.1. The time before marketing authorisation

The first set of root causes to investigate relate to delay before marketing authorisation. The granting of a centralised marketing authorisation by the European Medicines Agency (EMA) covering all EU countries eliminates the requirement to seek marketing authorisation for new therapies from each member state separately; however, the centralised process that is used for most innovative medicines still takes time.

The speed of the regulatory process

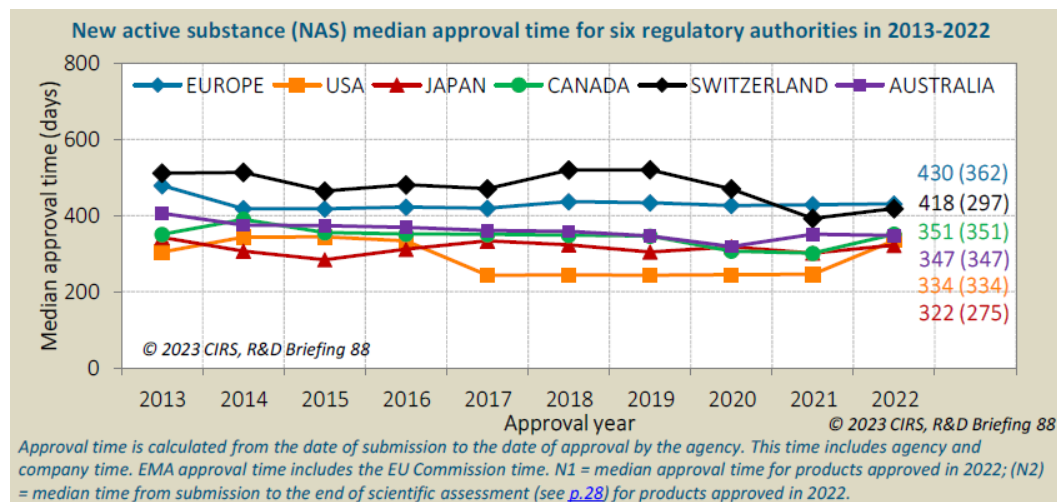
Although not captured in EFPIA’s W.A.I.T. Indicator, the time from application to granting of marketing authorisation has been examined in many papers. Looking at recent evidence regarding new, active substances, it is clear that the European regulatory process is slower

²⁰

Addressing Challenges in Access to Oncology Medicines, Analytical Report. OECD, April 2020.

than some international processes, particularly that of the United States (Figure 9 below).²¹ From the international comparisons shown in Figure 9, it appears that the approval timelines have generally converged in other regions of the world, whereas times in Europe have remained relatively unchanged; hence, Europe is lagging behind.

Figure 9: Comparison of length of time of market authorisation process



Source: CIRS (2023)²²

Many studies have focused on cancer medicines. On the basis of similar analyses over time, we observe that the speed of the regulatory approval process in Europe consistently lags behind that in other regions.

- For 29 cancer drugs approved by the EMA between 2006 and 2011, median approval time was shorter in the United States (US) (6.0 months) than in Japan and Europe (15.0 and 13.3 months, respectively). Breaking down the 13.3-month period, it comprises “active review” time (6.6 months), clock stops (4.2 months), and administrative time (2.1 months). This contrasts with the US, where the entire 6-month period is “active review” time. Researchers also found that companies file for market authorisation earlier in the US than in the EU but that this is a relatively small difference (1.7 months).²³
- Similar patterns were observed in another study focusing on 16 tyrosine kinase inhibitors approved by the US Food and Drug Administration (FDA) between 2001 and 2012. It found that while the average time spent on review and approval in the

²¹ This does vary by pathways. As reported in Rodier et al. (2019), the overall median approval time of the EMA for all the approved new active substances was about 423 days in 2019 compared to the official timelines of 210 days, with an average of 270 days for accelerated assessments, 481 days for conditional approvals, and 281 days for high-priority medicines. Rodier, C., Bujar, M., McAuslane, N. and Liberti, L. 2019. New Drug Approvals in Six Major Authorities 2009-2018: Focus on Facilitated Regulatory Pathways and Orphan Status. London, UK.

²² <https://cirsci.org/publications/cirs-rd-briefing-88-new-drug-approvals-in-six-major-authorities-2013-2022-focus-on-orphan-designation-and-facilitated-regulatory-pathways/> [accessed April 2024]

²³ Hartmann, M., Mayer-Nicolai, C. and Pfaff, O. (2013) Approval probabilities and regulatory review patterns for anticancer drugs in the European Union. *Critical Reviews in Oncology/Hematology* 87(2): 112–121

US (205.3 days) and EU (409.6 days) differed, the active review time was similar (205.3 days in the US and 225.4 days in the EU), and companies filed for market authorisation in both geographies within a mean 31.2 days of each other. The differences in total time are attributed to longer clock stops in the EU during the review process to collect additional information from sponsors and the time between the advisory opinion and the decision of the European Commission.²⁴

- A study with a broader geographic scope reported that median approval times for oncology drugs and immunomodulators from 2015 to 2019 were the longest for Swissmedic (450 days), followed by the EMA (419 days), the Australian Therapeutic Goods Administration (TGA) (352 days), Health Canada (345 days), the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) (284 days), and the FDA (239 days).²⁵
- The latest evidence suggests that these trends remain unchanged: a 2022 study found that between 2010 and 2019, the FDA approved 95% of new oncology therapies before the EMA, with a median delay to market authorisation in Europe of 241 days. The EMA's median review time was found to be 226 days longer than the FDA's. 72% of applications were filed with the FDA first, and 23% were first filed with the EMA. Applications were filed with the FDA with a median of 20 days earlier than with the EMA.²⁶

For other categories of medicine, the difference may be smaller, but the FDA is still faster than the EMA.²⁷

The studies described attribute some of the delay in Europe to the period between the Committee for Medical Products for Human Use (CHMP) opinion and the EC decision (as shown in Figure 10 **Error! Reference source not found.**). This is important to consider in light of proposed reforms to the General Pharmaceutical Legislation, which include reducing the official maximum time between the CHMP decision and EC decision from 67 to 46 days. However, even when combined with the EC proposal to reduce the EMA's maximum assessment time from 210 to 180 active review days, this amounts to a theoretical net reduction in time to approve a new medicine of only 51 days. Given that the above studies point towards a 100-to-250-day gap between the EMA and the FDA, a 51-day improvement in assessment speed is unlikely to be sufficient to close the gap between Europe and other regions.

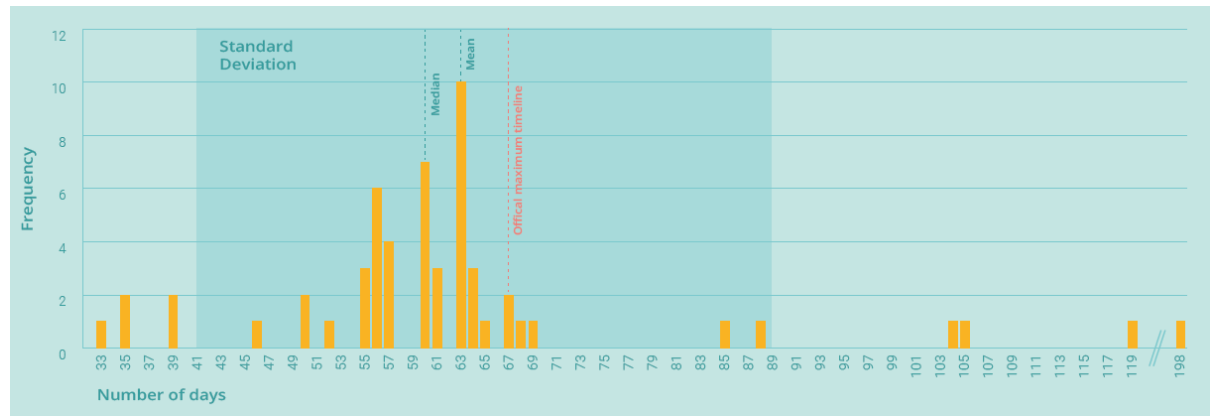
²⁴ Shah, R. R., Roberts, S. A. and Shah, D. R. (2013) A fresh perspective on comparing the FDA and the CHMP/EMA: approval of antineoplastic tyrosine kinase inhibitors. *British Journal of Clinical Pharmacology* 76(3): 396–411

²⁵ The Centre for Innovation in Regulatory Science (CIRS), 2020

²⁶ Lythgoe, M. et al. (2022) Cancer therapy approval timings, review speed, and publication of pivotal registration trials in the US and Europe, 2010-2019. *JAMA Netw Open* 5(6): e2216183.

²⁷ For example, "EMA and FDA comparison shows faster, and higher, approval rates in the US" <https://www.shakespearepharma.com/ema-and-fda-comparison-shows-faster-and-higher-approval-rates-in-the-us/>; and Zeukeng, M., Seoane-Vazquez, E. and Bonnabry, P. (2018). A comparison of new drugs approved by the FDA, the EMA, and Swissmedic: an assessment of the international harmonization of drugs. *European Journal of Clinical Pharmacology*, 10.1007/s00228-018-2431-7, 74, 6, (811-818)

Figure 10: Overview of timelines between CHMP opinion and EC decision



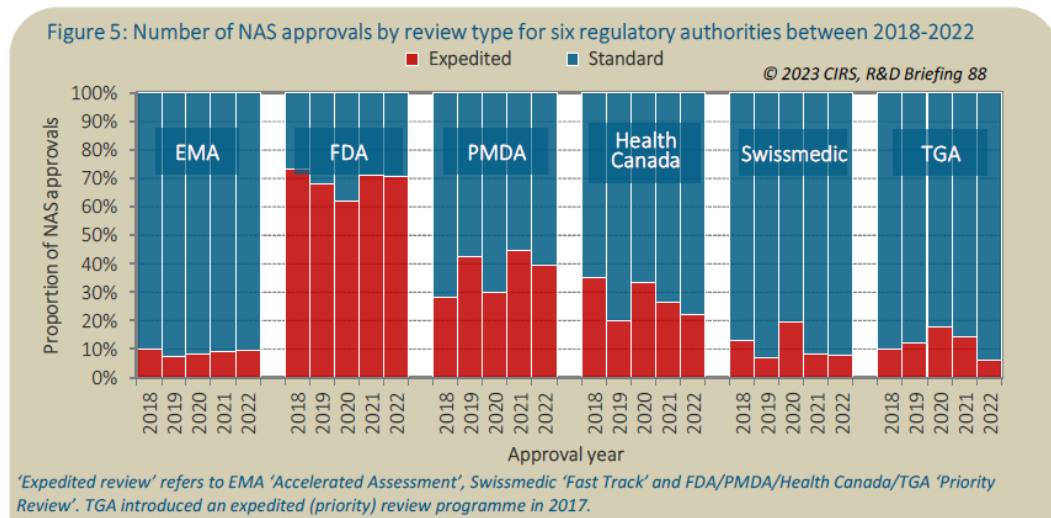
Source: Vintura (2021).²⁸ Timelines reflect oncology therapies (new molecular entities only) evaluated by the CHMP between 2016 and 2020.

Other evidence points towards underuse of expedited review pathways in the EU relative to other regulators that impacts average times to approval across therapy areas (see Figure 11). Analysis by CIRS shows that in 2022, 10% of new medicines approved by the EMA went through the accelerated assessment procedure. This is significantly lower than use of equivalent expedited review pathways by the PMDA (39%) and FDA (71%). The lower use of expedited reviews in Europe is attributed in part to the EMA’s denial of manufacturer requests for accelerated assessment (as occurred with 11 of the 52 new medicines approved in 2022).²⁹

²⁸ Vintura (2021) “Every Day Counts, Improving regulatory timelines to optimise patient access to innovative oncology therapies in Europe”. Available at: <https://www.efpia.eu/media/636486/improving-regulatory-timelines-to-optimise-patient-access-to-innovative-oncology-therapies-in-europe.pdf> [accessed March 2023]

²⁹ <https://cirsci.org/publications/cirs-rd-briefing-88-new-drug-approvals-in-six-major-authorities-2013-2022-focus-on-orphan-designation-and-facilitated-regulatory-pathways/> [accessed April 2024]

Figure 11: Comparison of use of expedited review pathways by different regulators



Source: CIRS (2023)³⁰

Even with the European Commission's proposals to streamline the EU's regulatory procedures, some argue that Europe is still losing ground in terms of priority of regulatory approval and that this is unlikely to improve in the future.³¹ However, even today there is often a significant delay caused by the marketing authorisation process.

Accessibility of medicines before marketing authorisation

In some countries, patients can access medicines before marketing authorisation.^{32,33} Funded early-access schemes represent temporary reimbursement pathways that ensure direct patient access to promising new treatments before regulatory approval where there is a clear unmet need.³⁴

Some countries have introduced early-access schemes specifically aimed at providing immediate patient access to products before a full marketing authorisation (MA) has been granted. Some countries, such as France and England, have a more systematic approach.

³⁰ <https://cirsci.org/publications/cirs-rd-briefing-88-new-drug-approvals-in-six-major-authorities-2013-2022-focus-on-orphan-designation-and-facilitated-regulatory-pathways/> [accessed April 2024]

³¹ For example, global regulatory timelines are changing over the last 10 years. EMAs have stayed relatively flat (increasing a little during the last year), while Japan's PMDA, the US's FDA, and China's NMPA have dramatically reduced their review timelines over the decade.

³² It is also possible that where a new indication for an existing product is not (yet) approved or covered, access to it may be possible through off-label prescribing.

³³ Formally, Hungary, Latvia, Austria, Germany, Denmark, Finland, the Netherlands, and Sweden do not require price obtainment from the competent authority before "market launch," according to EFPIA's Market Launch and Withdrawal Survey (May 2020). This is not the case in other countries. Indeed, there is a requirement to apply for reimbursement status before market launch is in effect in Italy, Czechia, Spain, Slovenia, and Portugal.

³⁴ In addition, most countries have named patient compassionate-use programs that might be offered to patients with life-threatening or seriously debilitating conditions or an area of unmet clinical need. These have recently been documented in Access to medicines in Europe: Delays and challenges for timely patient access, Bregtje Kamphuis, Anna-Maria Fontrier, Olina Efthymiadou, Jennifer Gill, Hana Salyga and Panos Kanavos | November 2021

For example, in France, products with high unmet need can be granted an “autorisation d’accès précoce” (AAP)³⁵ before receiving conditional market authorisation approval. Although the AAP was introduced only in 2021, it is not a new system but rather a reform of the rules on early access to unauthorised medicines that were first introduced in France in 1992.

More recently, somewhat comparable schemes have developed in other markets. An example is England’s “early access to medicines scheme” (EAMS). Unlike the French AAP scheme, a company that applies for EAMS must provide the medicine free of charge to the National Health Service (NHS) until full marketing authorisation is granted. Those patients who receive a free medicine during this EAMS period will continue to do so up to the point of a positive funding policy (e.g., HTA guidance, national funding policy, or local funding arrangements).³⁶

1.5.2. Delay between marketing authorisation and application for reimbursement

Once a medicine has received marketing authorisation, initiation of the reimbursement process can still be delayed for multiple reasons. For example, some countries want to wait for the formal EMA decision and/or reimbursement decisions in other countries before they begin their own reimbursement processes.

Even after the process is initiated, the length of the P&R process varies from country to country. Although the EU Transparency Directive (Directive 89/105/EEC) has set 180 days as the maximum time within which member states are to make P&R decisions, in practice this process may take much longer due to clock stops, a lack of adherence, or limited HTA capacity.

Initiation of the process

In a minority of markets, there is immediate access after marketing authorisation, at least for some products. For example, in Germany, the standard process gives manufacturers a temporary period of free pricing that enables access to a medicine that has been authorised by the EMA, almost from day one, avoiding the delay resulting from an ongoing HTA assessment and pricing negotiations.

However, in many markets the P&R process does not start automatically; instead, a company must file a submission to initiate the assessment process. The specific circumstances required to initiate the P&R process depend on the rules and varies by country. In some countries, it is possible for the process to begin before marketing authorisation, but other countries require a positive CHMP opinion or even a formal decision from the EC or a publication in the *Official Journal of the EU* before a product can be filed for P&R.

In certain cases, countries have filing requirements that dictate that a product cannot be filed for P&R until after other countries have completed their P&R process. This can cause

³⁵ This was introduced in July 2021 through the Social Security Financing Law for 2021 (LFSS 2021) and replaced the Autorisation Temporaire d’Utilisation, or “ATU.” When it is granted pre-marketing authorisation, the AAP replaces the cohort ATU.

³⁶ Office for Life Sciences. Gov.uk (2016). Guidance on Early access to medicines scheme (EAMS): task group and principles. 10 May 2016. <https://www.gov.uk/government/publications/early-access-to-medicines-scheme-eams-how-the-scheme-works/early-access-to-medicines-scheme-eams-task-group-and-principles>

delays in availability where manufacturers are prevented from filing for P&R and is most prevalent in CEE and Southern Europe. Here are two examples:

- In Bulgaria, a product can be filed for P&R only once a positive recommendation has been issued by the UK, France, Germany, or Sweden.³⁷
- In Greece, a product can be filed for P&R only if it is reimbursed in five of 11 specified countries.³⁸

In other cases, the process is dependent on other stakeholders and the marketing authorisation holder cannot file. This is changing for the better in some countries. For example, in Estonia, applications to the inpatient service list were previously made by clinicians, and, in principle, manufacturers were not able to initiate this process.³⁹ However, an amendment of Estonia's Health Insurance Act has resulted in the holder of the marketing authorisation of a medicinal product being able to initiate administration of the product.⁴⁰ Another example can be seen in Scotland, where manufacturers are proactively invited to submit newly approved indications to the Scottish Medicines Consortium after the country has conducted horizon scanning.⁴¹ In fact, the use of horizon scanning to identify and plan for the entry of innovative medicines into a health system is growing, both at the national level, as seen in countries such as Scotland, and the supranational level as a feature of cross-country collaborations such as BeNeLuxAI.^{42,43}

Illustrative timelines for the HTA process in various European countries are shown in the figure below. In some countries, such as England, the process can begin significantly before the marketing authorisation is obtained, while in others there is a delay even after publication of the marketing authorisation in the *EU Journal*.

³⁷ Malinowski, K. P., Kawalex, P., et al. (2020) Health technology assessment and reimbursement policy for oncology orphan drugs in Central and Eastern Europe. *Orphanet Rare Diseases*. 15(1):277.

³⁸ Greece: article 22 of Law 4633/2019: medicines with patent protection are subject to HTA in Greece only if they are reimbursed in five other countries with an HTA process from the following list: Austria, Belgium, France, Germany, Denmark, Spain, Netherlands, Italy, Portugal, Sweden, and Finland.

³⁹ Time to Entry for New Cancer Medicines: From European Union–Wide Marketing Authorization to Patient Access in Belgium, Estonia, Scotland, and Sweden. Ferrario, A. Health Policy Analysis. *Value in Health* 21(7): 809–821, 01 July 2018

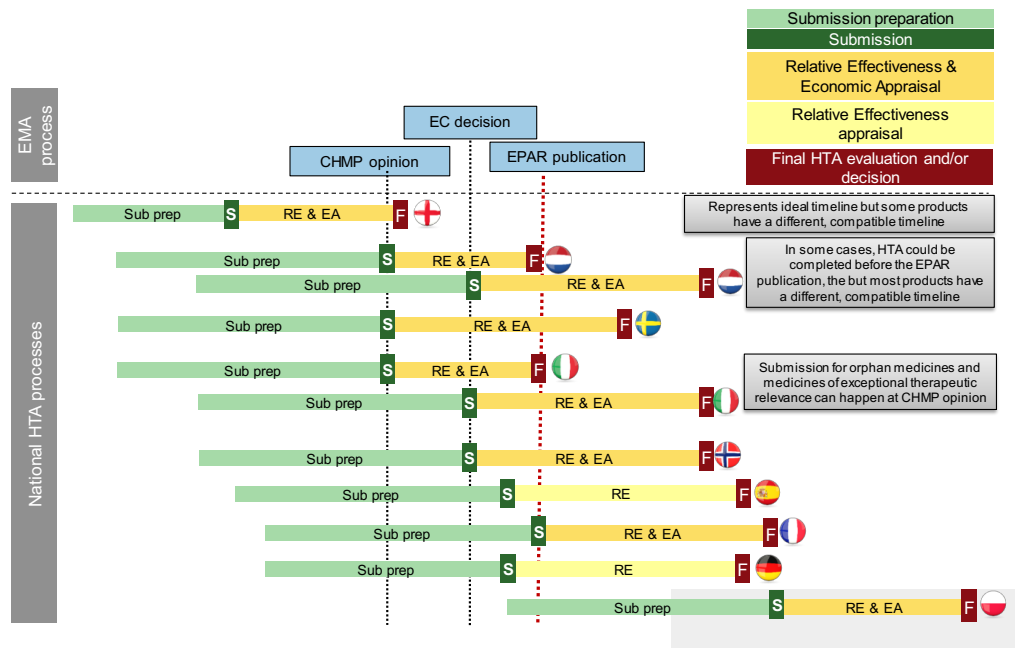
⁴⁰ Riigi Teataja (2022). Health Insurance Act. Available at <https://www.riigiteataja.ee/en/eli/520012014001/consolide>

⁴¹ Time to Entry for New Cancer Medicines: From European Union–Wide Marketing Authorization to Patient Access in Belgium, Estonia, Scotland, and Sweden. Ferrario, A. Health Policy Analysis. *Value in Health* 21(7): 809–821, 01 July 2018

⁴² EFPIA (2019) *Policy principles on cross-country collaborations on medicines' pricing and access*. Accessible at: <https://www.efpia.eu/media/412513/policy-principles-on-cross-country-collaborations-on-medicines-pricing-and-access.pdf>

⁴³ BeNeLuxAI is a cross-country collaboration, established in 2015, between Belgium, Netherlands, Luxembourg, Austria and Ireland. The countries work together to facilitate horizon scanning for upcoming innovative medicines.

Figure 12: Time until the reimbursement process can be initiated



Source: EFPIA; “EPAR” is short for “European public assessment report”

Leaving to one side the impact of national rules, two other key factors need to be taken into account.

- First, a significant amount of research has been done to illuminate the degree to which filing for P&R is influenced by external reference pricing. The resulting theory suggests that companies engage in launch sequencing—they file for P&R in higher-income countries first to prevent a spillover effect on price when countries reference the price of a medicine in a lower-income country with less ability to pay. A series of reports have documented the impact of external reference pricing on availability of innovative medicines.^{44,45}
- Equally, applying for P&R is time consuming. Every country requires a tailor-made dossier in the local language and in compliance with local rules. Although companies often have specialised groups to manage this process, internal activities still must be top priority. This issue is exacerbated for smaller companies, which may not have gone through the process before or perhaps do not have the same resources available in each country as larger companies, and for companies that have not launched a new medicine for some time. Figure 13 supports this finding by demonstrating that products manufactured by larger companies generally are more available.

44 Kanavos, P., Fontrier, A., Gill, J., & Efthymiadou, O. (2020) Does external reference pricing deliver what it promises? Evidence on its impact at national level. *Eur J Health Econ* (21): 129–151. Retrieved January 29, 2020, from <https://link.springer.com/article/10.1007/s10198-019-01116-4>

45 Incze, A., Kalo, Z., et al. (2022) Assessing the consequences of external reference pricing for global access to medicines and innovation: Economic analysis and policy implications. *Frontiers in Pharmacology*. 13:815029

Figure 13: Percentage of products available in EU countries, segmented by company size

Sorted by total availability (%) according to EFPIA W.A.I.T. (2019-2022 cohort)

Country	Top-20 global pharma	Other biotech and SME companies	Large company delta
	N = 71	N = 96	% above or below the country average reported in W.A.I.T.
Germany	94%	83%	6%
Italy	86%	71%	9%
Austria	86%	68%	10%
Switzerland	89%	56%	19%
Denmark	79%	55%	14%
France	69%	59%	6%
Czech Republic	82%	48%	19%
Spain	73%	53%	12%
England	61%	52%	5%
Netherlands	69%	44%	15%
Scotland	61%	49%	7%
Luxemburg	72%	40%	19%
Sweden	70%	35%	20%
Portugal	62%	41%	12%
Greece	79%	24%	32%
Belgium	62%	33%	16%
Bulgaria	59%	31%	16%
Finland	58%	31%	15%
Slovenia	61%	28%	19%
Poland	61%	27%	19%
Iceland	55%	23%	18%
Norway	54%	23%	18%
Cyprus	61%	9%	29%
Hungary	49%	16%	19%
Ireland	44%	17%	16%
Croatia	46%	7%	23%
Estonia	34%	7%	15%
Latvia	32%	8%	14%
Romania	30%	8%	12%
Slovakia	30%	8%	12%
Lithuania	18%	1%	10%
Serbia	15%	3%	7%
Bosnia and Herzegovina	17%	0%	10%
Macedonia	14%	1%	7%
Malta	1%	5%	-2%
Turkey	6%	2%	2%

Source: EFPIA Patients W.A.I.T. 2023, IQVIA analysis of company size, top-20 pharma defined by 2023 Q4 MAT total sales (Rx only) globally

However, the P&R process is not taxing only on industry resources; HTA bodies also have finite capacity to accept and review the applications they receive.⁴⁶ Logically, we assume this is especially the case in countries that have more nascent HTA bodies. However, it can also be a concern in countries with well-established organisations, and there are examples of backwards progress. For example, in Italy, the recent reorganisation of AIFA has resulted in the number of appointed HTA committee members decreasing from 20 to 10.⁴⁷ For this reason, companies are often inclined to not initiate an application until authorisation to enter the European market has been confirmed.

In 2022, EFPIA members committed to the creation of a European Access Hurdles Portal where marketing authorisation holders (MAHs) can provide timely information regarding the timing and processing of P&R applications in the various European countries, including

⁴⁶ O'Rourke, B. et al. (2019) The 'Top 10' Challenges for Health Technology Assessment: INAHTA Viewpoint. *Int J Technol Assess Health Care* 2020 36(1): 1–4. doi: 10.1017/S0266462319000825. Epub 2019 Nov 28

⁴⁷ AIFA (2024) <https://www.aifa.gov.it/en/commissione-scientifica-economica> [accessed April 2024]

the reasons the MAH has not filed in a particular market.⁴⁸ The second report documenting the results from the European Access Hurdles Portal has been published.⁴⁹

The speed of the national timelines and adherence

Most European countries have a set of rules around the timelines for decision-making on national pricing and reimbursement, but even when countries have such rules in place, compliance can be challenging. This results in delays and timing being unpredictable.

The length of time taken should, in theory, reflect the EU Transparency Directive (European Commission, 1988). The purpose of this directive was to ensure the transparency of measures that regulate P&R of medicinal products. It sets a strict maximum time of 180 days for reaching a national P&R decision. The clock starts ticking the moment a dossier is submitted and excludes time needed by companies to provide additional information (“clock stops”). However, input into the European Commission’s recent public consultation on the functioning of the Transparency Directive suggests that there are issues with its functioning and a need for the time limit to be “robustly enforced.”⁵⁰ The Transparency Directive puts the responsibility in the hands of national governments, whereas it is the responsibility of all stakeholders to facilitate reasonable interactions that ensure that evidence-based decision-making is possible within this time frame.

There is relatively little data on how much time elapses from the beginning of the national P&R process to its conclusion. Recent data on time to reimbursement of 35 novel oncology medicines are shown below (Figure 14 **Error! Reference source not found.**). Even after taking into account delayed initiation, there are significant differences across countries. This is consistent with initial findings from the European Access Portal, which distinguishes between delays in availability due to the initiation of the P&R process and due to the time taken to complete the P&R process.⁵¹ This is also consistent with criticisms of the functioning of the Transparency Directive, with the study finding that only in Germany was the 180-day timeline achieved for 100% of medicines; in other countries, a significantly smaller proportion of medicines were reimbursed within 180 days (51% in France, 29% in the UK and the Netherlands, 14% in Switzerland, 6% in Norway, and 3% in Belgium).⁵²

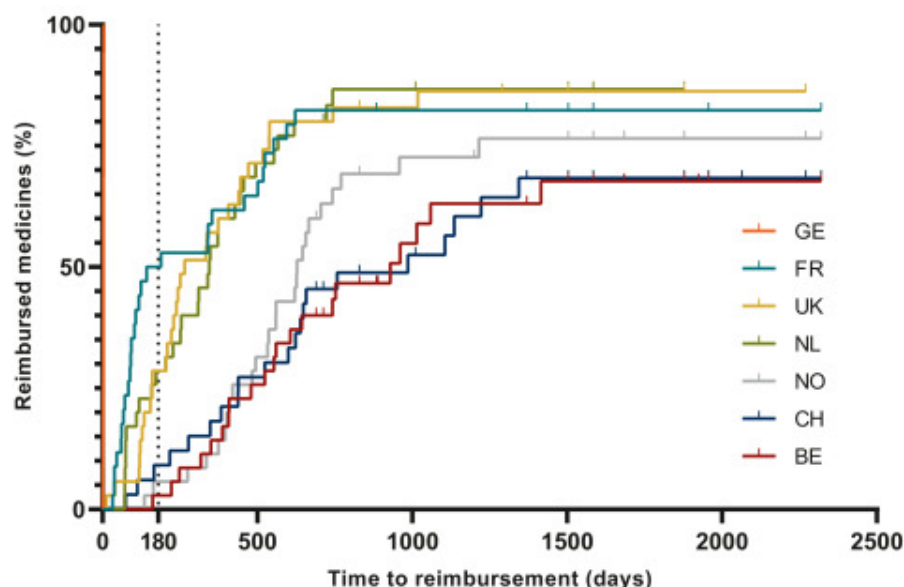
48 EFPIA (2022) “Addressing patient access inequalities in Europe: The Industry commitment to file pricing and reimbursement applications across Europe and the European Access Portal.” Available at: <https://www.efpia.eu/media/677156/addressing-patient-access-inequalities-in-europe.pdf> [accessed March 2023]

49 CRA, EFPIA (2024) European Access Hurdles Portal: Results from the second year of data collection
50 <https://www.apmhealthurope.com/story/18799/87672/no-discernible-progress-on-reviewing-the-eu-price-transparency-rules>
[accessed April 2024]

51 CRA, EFPIA (2023) European Access Hurdles Portal: initial results. Available at: <https://www.efpia.eu/media/677291/european-access-hurdles-portal-efpia-cra-report-200423-final.pdf> [accessed April 2024]

52 Post, H.C., et al. (2023) Time to reimbursement of novel anticancer drugs in Europe: a case study of seven European countries. *ESMO Open*. 8(2): 101208.

Figure 14: Time to reimbursement of novel oncology medicines in seven high-income European countries⁵³



Source: Post, H.C. et al. (2023)

There is evidence that tailored P&R approaches for different types of medicine can accelerate the P&R process. Countries with specialised P&R channels for orphan medicines, such as Finland, France, Norway, and Sweden, generally have faster availability of orphan medicines as a result.^{54,55} In some markets medicines dispensed in the hospital are immediately accessible, and the national reimbursement process applies only to medicines dispensed in community pharmacies. However, as specialist medicines have become an ever-larger part of the healthcare budget, more restrictions have been applied, as illustrated by the case of the Netherlands.⁵⁶ A lack of adherence to this specialist legislation can cause further delays in availability. For example, in Italy, the national P&R process for orphan drugs should conclude within 100 days under Italian law,⁵⁷ but it takes on average 413 days for new orphan medicines to become available to patients in Italy.⁵⁸

⁵³ Post, H.C., et al. (2023) Time to reimbursement of novel anticancer drugs in Europe: a case study of seven European countries. *ESMO Open*. 8(2): 101208.

⁵⁴ Detiček, A., Locatelli, I. and Kos, M. (2018) Patient Access to Medicines for Rare Diseases in European Countries. *ISPOR Value in Health*. 21(5): 553-560.

⁵⁵ Warttig, S., D'Souza, V. (2022) Analysis of Health Technology Assessment procedures and outcomes for orphan drugs. *ISPOR 2022*. Available at: https://www.ispor.org/docs/default-source/euro2022/warttigorphan-drug-ispor-eu-poster20-oct-2022upload-pdf.pdf?sfvrsn=40c238ee_0

⁵⁶ How is patient access to high-cost orphan drugs changing? <https://www.remapconsulting.com/patient-access-to-high-cost-orphan-drugs-remap-consulting/>

⁵⁷ Prada, M., Rossi, L. and Mantovani, M. (2020) Time to reimbursement and negotiation condition in Italy for drugs approved by the European Medicines Agency during the period 2014-2019. *AboutOpen* 7(1): 89-94

⁵⁸ *The Patient W.A.I.T. Indicator 2023 Survey*

1.5.3. Delays due to the value assessment process

A critical part of the P&R process is the value assessment process. Features of the value assessment process, including those that can lead to misalignment on evidence, misalignment between value and price, and countries having different perspectives on class competition and choice, are reported as some of the most prominent and complex factors resulting in delayed availability and lower rates of availability for innovative medicines.

Misalignment on evidence requirements

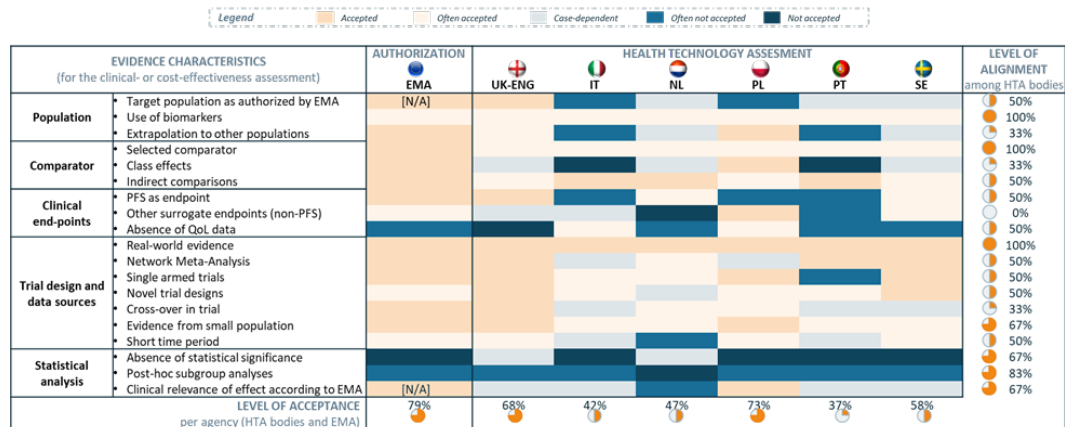
Misalignment takes place not only among industry, regulators, and HTA bodies but also between regulators and HTA bodies and among HTA bodies. Misalignment can be found in all assessment criteria, including patient population, comparators, trial design, end points, and statistical analysis.

Once the P&R process is initiated, one reason the national timeline extends beyond the 180 days set out in the Transparency Directive is clock stops due to requests for information or rejections during the HTA process. Countries have different evidence requirements during the assessment process, and this represents a challenge, as (1) evidence is developed at a global level so developing additional country-specific evidence can be time-consuming, and (2) evidence requirements are not always predictable (even with early dialogue processes that have developed in Europe over the last five years).

To illustrate the differences in evidence requirements, we can compare the evidence requirements of EMA and the HTA bodies in the six case-study countries from the Time to Patient Access project (see Figure 15**Error! Reference source not found.**). Based on desk research and interviews with agency representatives, for each agency the research assessed whether 19 different characteristics would be accepted as convincing evidence.

The level of alignment is highest for the use of biomarkers and real-world evidence (RWE), for example. These elements are “often accepted” by all HTA bodies. The level of alignment is lowest when HTA bodies are asked for acceptance of surrogate endpoints other than progression-free survival (PFS). As illustrated in Figure 15**Error! Reference source not found.**, every agency looks at the use of surrogate endpoints in a different way: they are accepted in Poland and often accepted in Sweden; not accepted in the Netherlands, and often not accepted in Portugal. England and Italy determine acceptance on a case-by-case basis.

Figure 15: Evidence requirements vary between agencies, prolonging national discussions and decision-making



Source: [Time to Patient Access](#), Vintura (July 2020). The grey colour code reflects acceptance on a case-by-case basis. The blue colour code (“often not accepted”) and lighter orange colour (“often accepted”) also reflect a certain level of unpredictability.

This is consistent with findings in the literature that only around 40% of HTA agencies globally have guidelines that make specific reference to the consideration of surrogate endpoints.⁵⁹ For slowly progressive diseases, such as Alzheimer’s, and for those diseases for which pharmaceuticals have already greatly increased survival rates, it is becoming increasingly difficult to design clinical trials with gold-standard endpoints. This has led to calls for greater acceptance of surrogate endpoints to facilitate better availability of innovative medicines. However, HTA agencies are often reluctant to consider these surrogate endpoints, which results in unavailability and delays. Analysis of HTA of oncology medicines in Germany, UK, and France indeed finds that the number of submissions that rely on surrogate endpoints are increasing but that this is associated with negative HTA outcomes.⁶⁰

From January 2025, the implementation of the EU HTA regulation, and specifically the Joint Clinical Assessment (JCA), could go some way to ensuring greater alignment between manufacturers and national HTA bodies and between all national HTA bodies across Europe. If successful, the EU HTA could theoretically support a reduction in delays resulting from misalignment of evidence requirements. However, a recent report highlighted that country misalignment on evidence requirements could prevent the EU HTA regulation from improving access to innovative oncology medicines, as the different PICO requirements for member states resulted in a wide assessment scope and an extended process.⁶¹

⁵⁹ Grigore, B. *et al.* (2020) Surrogate Endpoints in Health Technology Assessment: An International Review of Methodological Guidelines. *Pharmacoeconomics* 38: 1055-1070.

⁶⁰ Petrou, P., *et al* (2022) The notion of Surrogacy in Health Technology Assessment: an insight in the process of Germany, UK and France. *Journal of Medical Economics*, 25(1), 321-323

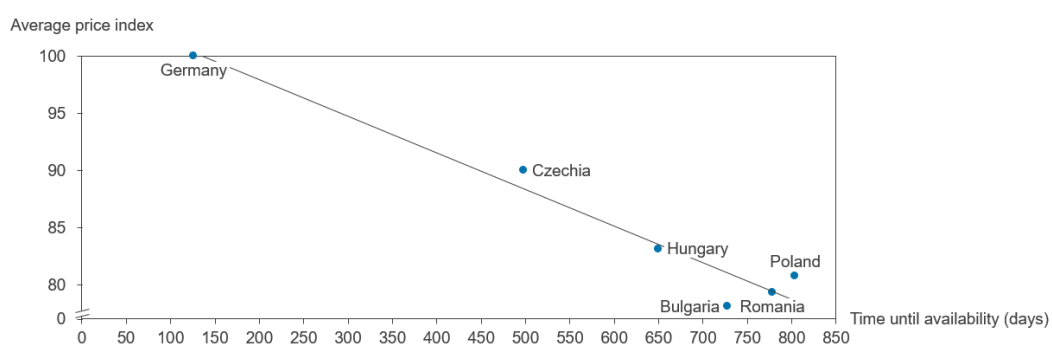
⁶¹ EFPIA (2024) EU HTA regulation for oncology medicines: learnings from a simulation on the impact of proposed EUnetHTA21 methods. Accessible at: <https://www.efpia.eu/media/qrjah2ij/efpia-evidera-research-on-eunethta21-methods.pdf>

Misalignment of value and price

Next, even if there is agreement on the evidence of the value of a medicine, countries have different levels of income and hence ability to pay. Decision-makers are faced with the enormous challenge of striking a balance between fast patient access, uncertainty about real-world value, and a reasonable price reflecting the (potential) value.

The relationship between price and delays is debated. Analysis of list prices suggests a simple negative relationship between price indices and time until availability (see Figure 16), which indicates that countries with lower prices may have to wait longer for innovative medicines to become available. This is consistent with analysis of external reference pricing and launch sequencing that reveals that manufacturers may at first avoid launching in countries with lower prices to prevent unsustainable spillover effects. However, this analysis is too simplistic; it fails to account for the numerous confounding factors that impact availability. For example, high-price countries may have quicker diffusion and greater usage. Other studies have failed to find a relationship between delays and prices, suggesting that expected prices do not affect the speed of launch.⁶²

Figure 16: A comparison of average list price (% DE price) versus time until availability (days)



Source: *The Patient W.A.I.T. Indicator 2023 Survey; Pharmaceutical Technology*⁶³

Some mechanisms have been introduced with the goal of minimising costs to the healthcare system but the effect of delinking value and price. For example, clawbacks, which require manufacturers to pay back a share of their revenue from a product, have been directly identified as delinking price and value. They undermine the value assessment process and could be responsible for precipitating a decrease in the rate of availability of innovative medicines. Another mechanism intended to lower healthcare costs, external reference pricing, is also inconsistent with a value-based approach.⁶⁴

There is broad consensus that prices should reflect the ability to pay. Where prices are higher than the perceived value or affordability, delay as the price is negotiated is inevitable.

⁶² Time to Entry for New Cancer Medicines: From European Union–Wide Marketing Authorization to Patient Access in Belgium, Estonia, Scotland, and Sweden. Ferrario, A. *Health Policy Analysis. Value in Health* 21(7): 809–821, 01 July 2018

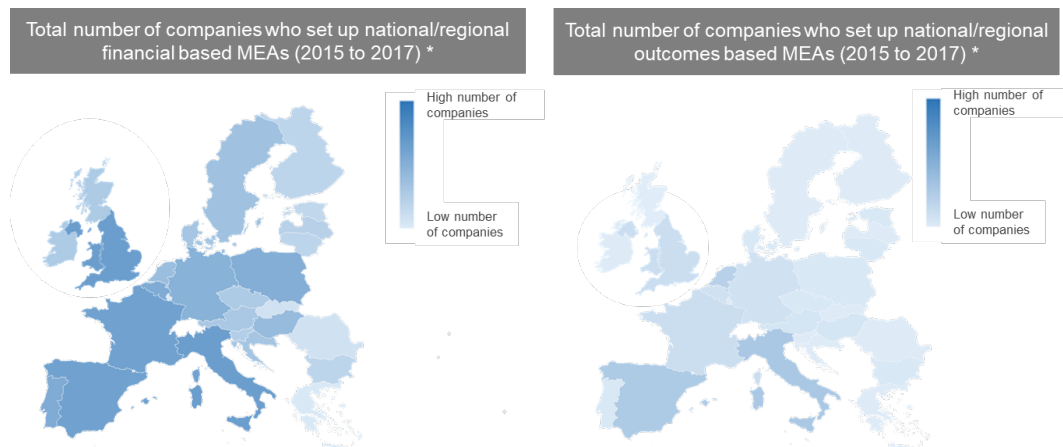
⁶³ Labban, M. (2021) Reference pricing in CEE countries puts downward pressure on prices. *Pharmaceutical technology*. Accessible at: <https://www.pharmaceutical-technology.com/pricing-and-market-access/reference-pricing-cee-countries-pressure-prices-html/?cf-view> [accessed April 2024]

⁶⁴ EFPIA (2023) A value-based approach to pricing. Accessible at: <https://www.efpia.eu/media/677284/a-value-based-approach-to-pricing-2.pdf>

External reference pricing (discussed above) complicates this; the agreed price needs to reflect how it will be used outside the country in addition to its alignment with the national HTA body's assessment of value.

The ability to agree novel payment mechanisms (which can offer a means to align price with value) varies considerably around Europe (see Figure 17 **Error! Reference source not found.**). This is particularly the case in Central and Eastern Europe, where we observe the largest delays. There are also disparities across therapy areas that are likely to feature in novel payment mechanisms, with recent analysis showing that more than 50% of agreements in Europe relate to oncology.⁶⁵

Figure 17: The use of managed entry agreements (MEAs) across Europe



Source: EFPIA "MEAs and innovative pricing models: Real world experience" Final Report 2018

The value assigned to product differentiation and choice

The value that countries place on the availability of a particular medicine also varies. Countries have different numbers of patients with a particular condition (some countries may have very few), and approaches to treatment vary, with some countries favouring surgical approaches rather than therapeutic interventions, for example. So clinical and epidemiological factors affect the degree to which countries have an unmet need and therefore the degree to which these medicines are prioritised in P&R process and value assessments.

Another dimension should be considered: physician choice and the value of competing medicines. Countries take different approaches to determining the value of class competitors. Some countries believe that physicians should have access to all products on the market so they can provide patients with the best products for them and have clinical freedom. Equally, competition between innovative medicines is encouraged in some markets, with the follow-on products in a class being encouraged because they can lead to competition and better value for the payer. On the other hand, some countries have favoured the approach of choosing a preferred product, sometimes through a rigid procurement process that allows them to select a single manufacturer at least for a period of time. Where this is the case, is it unsurprising that we see access to only a subset of

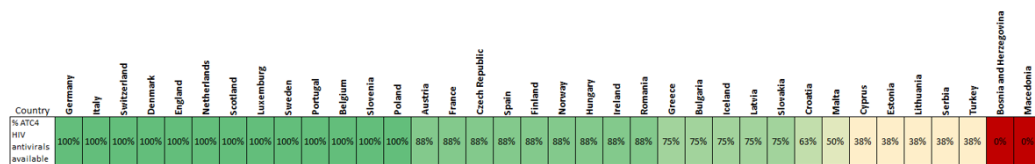
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Ciulla, M. et al (2023) Healthcare systems across Europe and the US: The Managed Entry Agreements Experience. *Healthcare*. 11(3), 447. Accessible at: <https://www.mdpi.com/2227-9032/11/3/447>

products. For example, from tenders for innovative medicines within an indication that Nordic countries have conducted, we can see that they place less value on innovative medicines that do not offer obvious therapeutic value compared to what is already available.⁶⁶ This may explain the decline in rates of availability observed in the Nordics over recent years.⁶⁷

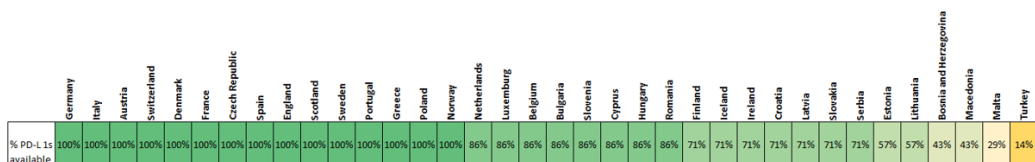
Given that the number of options varies in different ATC4 classes, we would expect to see differences in availability of products. This expectation is validated by the evidence, as shown by Figure 18 **Error! Reference source not found.**, which presents the percentage of HIV antivirals (J5C9) and PD-L1s available in each country. Despite availability varying significantly across the European countries, the vast majority of countries have access to at least one HIV antiviral medicine, and all countries have access to at least one PD-L1.

Figure 18: Number of products available in a therapeutic class (the example of HIV antivirals and PD-L1s)



Scale:
At least 1/8 product in the ATC4 class available = green (graduated)
0/8 products available = red

Source: EFPIA Patients W.A.I.T. (2023), IQVIA ATC4 class (J5C9, HIV antiretrovirals, n=8)



Scale:
At least 1/7 product in the ATC4 class available = green (graduated)
0/7 products available = red

Source: EFPIA Patients W.A.I.T. (2023), IQVIA ATC4 class (PD-L 1s, n=7)

The number of products available in a therapeutic class is therefore likely to reflect the value that different countries put on competing products and the degree to which payers perceive a loss due to lack of choice.

1.5.4. Health system constraints and resources

The fourth category of root causes relates to the health system and its funding and infrastructure. To understand availability and delay, we need to take into account health

⁶⁶ Norway has gone a step further, including a 'need' clause in the National Regulatory procedure that dictates only those drugs that add therapeutic value should be accepted. Hobaek, B., LIE, AK. (2019) Less is more: Norwegian drug regulation, antibiotic policy and the 'Need Clause'. *Milbank Q.* 97(3):762-795. Accessible at: <https://doi.org/10.1111%2F1468-0009.12405>

⁶⁷ EFPIA W.A.I.T Indicator (2023)

system constraints and resources, particularly insufficient budgets to implement decisions and the infrastructure for diagnosis.

Insufficient budget to implement decisions

Within the EU, we clearly have countries with very different levels of income, with GDP per capita varying from €33,000 to €136,000 per annum.⁶⁸ They also have made different decisions regarding the amount they invest in health care. The data from the OECD clearly show the European differences in economic context:

- Relative healthcare spending as a percentage of overall GDP is twice as high in Germany and France (12.7% and 12.1% respectively) as in Romania (6.5%).⁶⁹
- Relative pharmaceutical expenditures as a percentage of overall GDP are more than four times higher in Greece and Malta (2.5% and 2.4%, respectively) than in Denmark and the Netherlands (0.61% and 0.72% respectively).⁷⁰
- Absolute healthcare spending ranges from approximately €2,200 per capita in Romania to €7,500 per capita in Germany.⁷¹

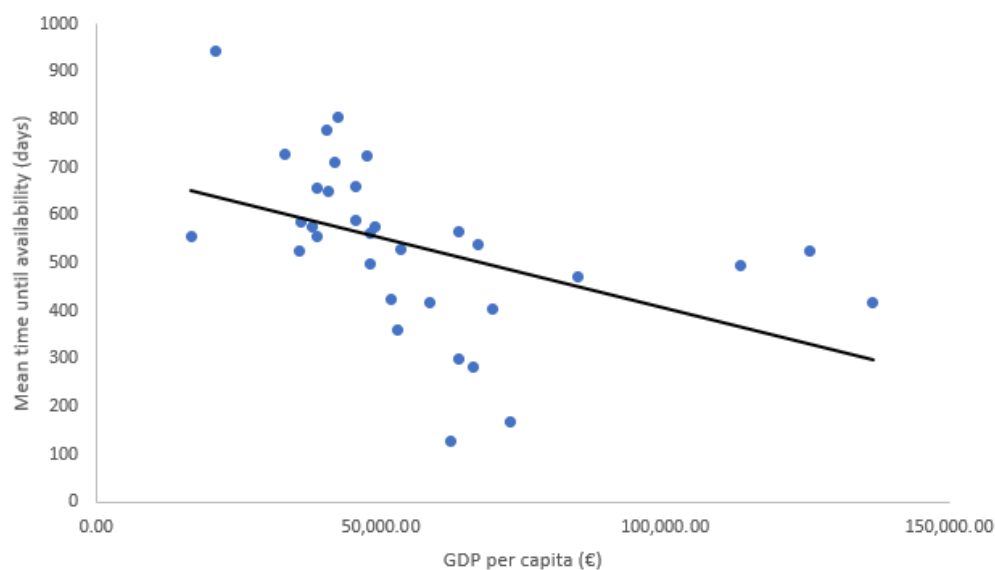
Given the differences in income and spending on health care and medicines, it is unsurprising that the prioritisation of health technologies varies across European countries and, in turn, that access to different forms of health care varies.

68 OECD. (2024). Gross domestic product (GDP). Available at: <https://data.oecd.org/gdp/gross-domestic-product-gdp.htm> [accessed April 2024]

69 OECD. (2024). Health Spending. Available at: <https://data.oecd.org/healthres/health-spending.htm#indicator-chart> [accessed April 2024]

70 OECD. (2024). Pharmaceutical Spending. Available at: <https://data.oecd.org/healthres/pharmaceutical-spending.htm> [accessed April 2024]

71 OECD. (2024). Health Spending. Available at: <https://data.oecd.org/healthres/health-spending.htm#indicator-chart> [accessed April 2024]

Figure 19: Relationship between time to availability (delays) and GDP per capita

Source: *The Patient W.A.I.T. Indicator 2023 Survey, OECD 2023*

As shown in the figure above, we do find a negative relationship between income and delays (clearly, many other factors also come into play). This result is consistent with the broader economic literature. Indeed, many papers show that the impact of the size of the market remains after many other factors are accounted for. For example, Costa-Font et al. observed a significant and robust market size effect: the launch time of new pharmaceutical products decreases as market size increases.⁷²

Population size can be a compounding factor. We have countries with a relatively high proportion of pharmaceutical expenditure as a proportion of GDP but a very small population size (such as Malta, with 2.4% of GDP spent on pharmaceuticals but a population of only 500,000).

Diagnosis, supporting infrastructure, and relevance to patients

Existing health infrastructure is a barrier to access in many European countries. Even after reimbursement, healthcare systems may face difficulties absorbing and using a new therapy optimally due to the need for high-quality health facilities, diagnostic centres, and health personnel.

Many infrastructure-related barriers make applying for reimbursement for a medicine in some markets unrealistic. Healthcare system infrastructure varies significantly across Europe (for example, hospital-bed density ranges from 221 beds per 100,000 inhabitants in the Netherlands to approximately 600 in Germany).⁷³ The infrastructure disparity is particularly evident with respect to highly specialised or orphan medicines:

⁷² Costa-Font, J., McGuire, A. and Varol, N. (2015) Regulation effects on the adoption of new medicines. *Empirical Economics* 49(3): 1101–1121. ISSN 0377-7332

⁷³ Eurostat (2024) Curative care beds in hospitals, 2021. Available at: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Healthcare_resource_statistics_-_beds [accessed April 2024]

- Accurate, timely diagnosis depends on accessible screening and diagnostic programs and services, which in turn depend on the infrastructure and expertise (e.g., the number of geneticists) available.⁷⁴ The degree to which countries have adopted widespread screening or targeted diagnosis of at-risk patients varies significantly.
- Even where diagnostic programs exist, access to diagnostic testing can be limited. For example, a recent study found that uptake of multi-biomarker testing for precision oncology varies from 0% to over 50% across European countries (Figure 20).⁷⁵ Country-level studies have identified the absence of public funding for testing as the main barrier to uptake.⁷⁶ A recent analysis by the European Society for Medical Oncology (ESMO) found that the lack of reimbursement for diagnostic tests was a main barrier to uptake of advanced biomolecular oncology technologies in 59% of cases, albeit with high heterogeneity across Europe.⁷⁷ Therefore, appropriate reimbursement for (newly approved) diagnostics is needed.
- Diagnosis requires investment in reimbursement of diagnostics and appropriate investment in testing facilities, and it also requires investment in physician education (and a focus on paediatricians) and an effective referral process.
- Given the small number of patients needing highly specialised or orphan medicine, expertise ideally should be concentrated in Centres of Excellence (CoEs), but these facilities are not evenly developed across European markets. This is an especially important consideration with regard to advanced-therapy medicinal products (ATMPs), which require highly specialised administration not possible in every country.

⁷⁴ Dharssi, S., Wong-Rieger, D., Harold, M. and Terry, S. (2017). Review of 11 national policies for rare diseases in the context of key patient needs. *Orphanet Journal of Rare Diseases* 12(1): 63

⁷⁵ Normanno, N. et al. (2022) Access and quality of biomarker testing for precision oncology in Europe. *European Journal of Cancer* 176: 70-77.

⁷⁶ Mestre Ferrandiz, J. et al. (2023) Biomarkers as a driver of precision medicine in oncology

⁷⁷ Bayle, A., et al. (2023) ESMO study on the availability and accessibility of biomolecular technologies in oncology in Europe. *Annals of Oncology*. 34(10):934-945

Figure 20: Access to precision oncology biomarker testing in Europe

(A) Single biomarker test access (B) multi-biomarker test access (C) biomarker test quality



Source: Normanno et al. (2022)⁷⁸

In many countries, the availability of scientifically robust epidemiological data for individual rare diseases varies greatly; such data may not be available at all.⁷⁹ The result can be a vicious cycle: a lack of country-specific epidemiological data contributes to a lack of appropriate health resource prioritisation decisions and little attention being given to the need to develop rare-disease diagnostic programs. The lack of a developed coding nomenclature for rare diseases also creates challenges, particularly for healthcare systems, which need to map out their specialised healthcare services and budget impact.⁸⁰

As a result—given that the number of patients with rare diseases may be very low and finding these patients may be difficult—ensuring appropriate use and pharmacovigilance is challenging and applying for reimbursement is not currently commercially viable.

Unsurprisingly, for some orphan medicines, availability across Europe is low. But even where products are not available on the national reimbursement list, the industry works with other stakeholders to ensure access for patients. There is evidence of the use of compassionate-use programmes across Europe.⁸¹ And patient-advocate groups have stressed a need for effective cross-border healthcare to support patients needing access to highly specialised care in other countries.⁸²

⁷⁸ Normanno, N. et al. (2022) Access and quality of biomarker testing for precision oncology in Europe. *European Journal of Cancer* 176: 70-77.

⁷⁹ De La Paz, M. P., Taruscio, D. and Groft, S. C. (2017). *Rare Diseases Epidemiology: Update and Overview*. Springer International Publishing (Verlag)

⁸⁰ Rath, A., Bellet, B., Oly, A., Gonthier, C. and Aymé, S. (2014) How to code rare diseases with international terminologies? *Orphanet journal of rare diseases* 9(1): O11

⁸¹ Balasubramanian, G. An overview of Compassionate Use Programs in the European Union member states, *Intractable Rare Dis Res.* 2016 Nov; 5(4): 244–254. doi: 10.5582/irdr.2016.01054

⁸² Eurordis (2021) Rare Diseases Europe responds to the evaluation of patients' rights in cross-border healthcare – and provides recommendations to improve the system. Available at: https://download2.eurordis.org/documents/pdf/CBHC_evaluation_standalone_response.pdf [accessed April 2024]

1.5.5. Delay from national to regional approval

Most studies on availability and delays focus on time to national reimbursement. In reality, there are multiple layers of decision-making processes. In some countries, reimbursement decisions must be made at all levels, from national to regional to the local hospital level, thus prolonging the time before patients can access treatments.

Multilayer decision-making processes

European countries have different ways of organising their decision-making processes. Some countries, such as Iceland and Croatia, organise price negotiations, assessment, appraisal, and budget allocation on a national level. Others organise these decisions partly at the national level and partly at the regional level. In most European countries, price negotiations, assessment, and appraisal take place on a national level but budgets are allocated by healthcare insurers (a single-payer institution or multiple health insurers) or hospitals.

To illustrate this, many researchers examine the situation in Italy. For example, one paper reported that both timing and the number of drugs available for patients varied widely from region to region. The mean best regional time (defined as the average number of days from AIFA market authorisation, as published in the GU, to the first purchase date in the first Italian region) was 29 days. The longest regional time (the number of days between GU and the first purchase in the last region for which data are available to date (July 2016)) was 293 days.⁸³ More recent analyses have revealed little improvement over the last seven years. A 2023 study found that the average time to regional access following the national decision in Italy was 65 days and that this ranged from 1 to 773 days, depending on the medicine and the region. Patients in northern regions such as Lombardy were frequently found to have faster access to new medicines than those in southern regions such as Molise.⁸⁴

Although the academic literature has focused on Italy, these findings apply to many markets in Europe.

1.6. Availability is not access

Even once a medicine is on the public reimbursement list and has navigated any regional processes, patients may not have access to it. The Time to Patient Access⁸⁵ project identified remarkable differences in the use of new oncology therapies once reimbursement is in place. In a study of access in 16 countries, 12 months after reimbursement, average access to 13 recently launched therapies ranged from 61% to 0.3%.

Many other barriers affect usage of medicines:

83 Rada, M. (2017) Timeline of Authorization and Reimbursement for Oncology Drugs in Italy in the last three years.

84 Mastroianni, G., Viola, V. and Perrone, F. (2023) Regional Access Timelines in Italy: Factors Affecting Speed and Equity. Available from: <https://www.ispor.org/docs/default-source/euro2023/isporeurope23mastroiannihpr99poster131491-pdf.pdf> [accessed April 2024]

85 Vintura (July 2020) "Every Day Counts" Available at: <https://www.efpia.eu/media/578013/every-day-counts.pdf>

- An additional delay on top of the P&R period is attributed to the time between the P&R decision and publication in the national gazette (journal). The following are examples:
 - Publication, necessary for final access in Belgium, adds an additional level of bureaucracy and a delay of two to three months.
 - In Italy, delay is common between a reimbursement decision for a new medicine and the final step of the national P&R process: publication of the decision in the *Gazzetta Ufficiale (Official Gazette)*.
 - In Hungary, although officially the reimbursement decision for a new medicine should be taken within 90 days, updating of the reimbursement list is ad hoc.⁸⁶ Yet in both the inpatient and outpatient sectors, a medicine must be included on the reimbursement list before it is used.⁸⁷
 - In Bulgaria, the reimbursement list is updated on a predictable schedule: once a year in January.⁸⁸ Therefore, if the P&R process for recently launched medicines does not conclude by December of any given year, reimbursement will be delayed by another full year.
- Clinical guidelines do not always include the most recent therapeutic innovations, even in larger Western European countries. For example, in France, the French National Authority for Health's guidelines for diabetes were last updated in 2013, despite the reimbursement of many new medicines and drug classes since then.⁸⁹ The absence of up-to-date clinical guidelines may cause delays for two reasons: first, a new medicine may not be picked up in horizon scanning, leading to a delay in decision-making by HTA bodies, and second, prescribers may resist beginning to use new therapies due to a lack of clarity on the positioning of the new therapy in the treatment pathway. This is illustrated below for new personalised oncology medicines (Figure 21 **Error! Reference source not found.**).

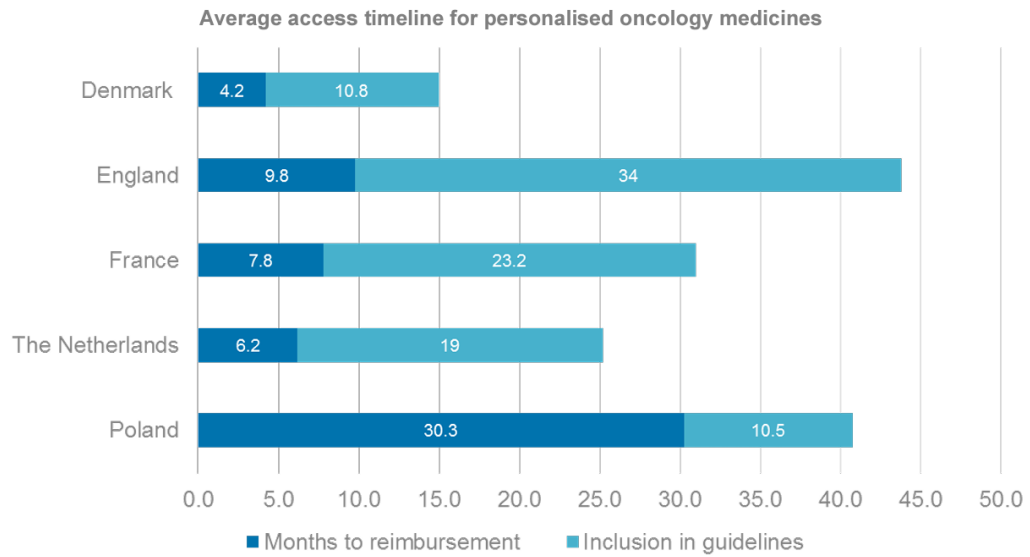
86 Kawalec, P. et al. (2017) Pharmaceutical Regulation in Central and Eastern European Countries: A Current Review. *Front Pharmacol* 8:892.

87 WHO (2018) "Medicines reimbursement policies in Europe" Available at: https://www.euro.who.int/_data/assets/pdf_file/0011/376625/pharmaceutical-reimbursement-eng.pdf [accessed March 2023]

88 Kawalec, P. et al. (2017) Pharmaceutical Regulation in Central and Eastern European Countries: A Current Review. *Front Pharmacol* 8:892.

89 Haute Autorité de Santé (2013) "Stratégie médicamenteuse du contrôle glycémique du diabète de type 2" Available at: https://www.has-sante.fr/jcms/c_1022476/fr/strategie-medicamenteuse-du-contrôle-glycemique-du-diabete-de-type-2 [accessed March 2023]

Figure 21: Average access timeline for personalised oncology medicines



Notes: Average access timeline from first-in-class PM in NSCLC, Melanoma and Ovarian Cancer (gefetinib; crizotinib; vemurafenib; pemprolizumab; olaparib)

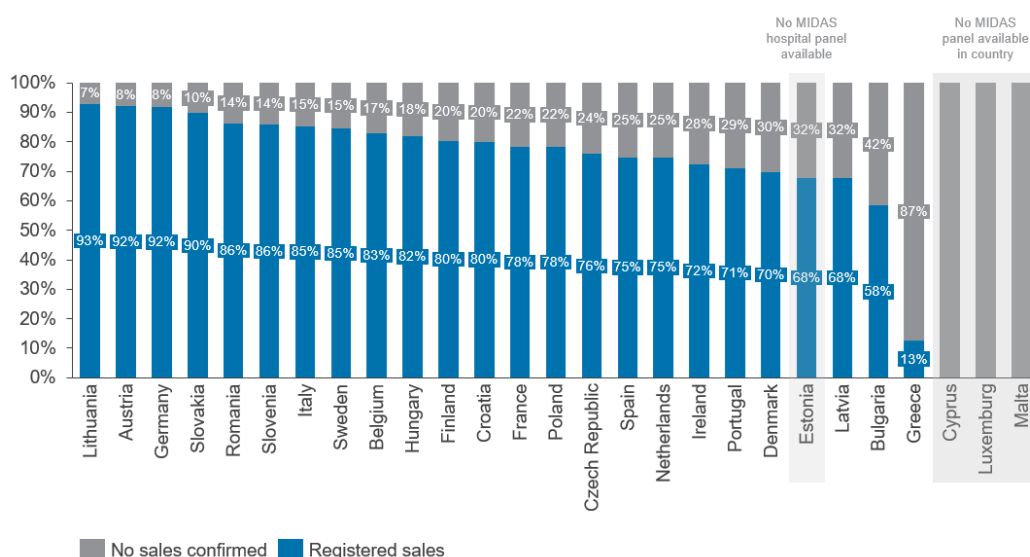
Source: EBE Personalised Medicine Report (2018)⁹⁰

- In other cases, a medicine is on the reimbursement list but budgets are not allocated for its use or it is not recommended. As a result, even once the full process has been completed and a medicine is potentially available on the market, there is no guarantee that it can be used. For example, patients have access to only 76% of products available in the Czech Republic (see Figure 22). Unsurprisingly, not all companies choose to apply for reimbursement in these markets.

90

CRA, EBE, EFPIA (2018) "An evidence-based analysis to characterise the benefits of personalised medicines to patients, society and healthcare systems" Available at: <https://www.efpia.eu/media/362039/cra-efpia-ebe-the-benefits-of-personalised-medicines-to-patients-society-and-healthcare-systems-final-slide-deck-2-july-2018.pdf> [accessed March 2023]

Figure 22: Percentage of available products with no recorded sales in the EU



Source: IQVIA MIDAS sales data 2016–2023. Analysis includes all available products (2019–2022). “Sales” is defined as available in WAIT indicator and showing EU sales in IQVIA MIDAS. “No sales” is defined as available in WAIT indicator and showing no EU sales in IQVIA MIDAS since 2015. Some countries in this analysis are not covered by IQVIA data or do not cover the hospital channel (i.e., coverage is retail only).

1.7. The impact of delayed access to innovative medicines

The impact of delays falls on patients, the healthcare system, and society. It is difficult to quantify that impact, but it undoubtedly leads to⁹¹

- Higher mortality and avoidable deaths;
- Lost quality of life for patients and their families and friends;
- Other healthcare costs that could have been avoided with newer treatments and a knock-on impact on other patients; and
- Loss of productive employment and ultimately a cost to the economy.

The scale of the potential impact of reducing delays can be illustrated by looking at potential efficiencies. For example, if the length of time between CHMP opinion and EC decision could be reduced by 12 days, the result would be 3,300 years of potential life (YPL) saved; if it were reduced by 15 days, 4,200 YPL.⁹²

1.8. Policy solutions to improve availability of innovative medicines

As discussed in this paper, the unavailability of medicines and delays are multifactorial. They are rooted in medicines access systems and processes in member states and corresponding impacts on commercial decision-making. Factors include a slow regulatory

⁹¹ Achieving equal and timely access to innovative anticancer drugs in the European Union (EU): summary of a multidisciplinary CECOG-driven roundtable discussion with a focus on Eastern and South-Eastern EU countries <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6863652/>

⁹² Vintura, November 2021, Every Day Counts, Improving Regulatory Timelines to Optimise Patient Access to Innovative Oncology Therapies in Europe

process, late initiation of market access assessment, duplicative evidence requirements, reimbursement delays, and local formulary decisions. All stakeholders aspire to all patients across the EU having timely and equitable access to safe, effective, and affordable medicines,⁹³ and the issues can be resolved only by stakeholders working together. To bring stakeholders together to discuss the root causes and consider policy solutions and how they could work in practice, EFPIA has called for a high-level multi-stakeholder forum on access to innovation—building on the ongoing Novel Medicines Platform being developed under the aegis of WHO Europe—and made a series of commitments, including filing P&R applications in all EU countries no later than two years after EU market authorisation, provided that local systems allow it.⁹⁴ This commitment reflects the joint ambition of industry and society to make innovation for unmet health needs available for patients and health systems across Europe as soon as possible. However, no single commitment, or indeed regulatory requirement, can address unavailability and delay, and a package of policy proposals is needed.

Reflecting the root causes, proposals are required in five areas:

Proposals to speed up the regulatory process to deliver safe and high-quality diagnostics, vaccines, and treatments to patients as fast as possible

There is a shared aspiration to reduce regulatory approval times in Europe and bring them in line with international best practice.⁹⁵ Several areas for action within the existing legislative framework exist to address this: encourage the use of new types of clinical trials; allow greater use of data from real-world use of medicines; allow ongoing dialogue between the developer and the regulator about a treatment throughout the development continuum (dynamic regulatory assessment), and simplify how medicines and other healthcare products are regulated, e.g., by closing the gap for GMO and combination products compared to medicinal products and streamlining the biomarker validation process.

Evaluation and revision of the basic pharmaceutical legislation (Dir 2001/83 and Reg 726/2004) and consolidation with other regulations would provide an opportunity to reinforce expertise-driven assessment and enable a more agile, centralised authorisation framework. The European Commission's proposals include simplification of the structure of the EMA's scientific committees, reduction of the scientific evaluation period from 210 days to 180 days, reduction of the period between the CHMP opinion and the final decision to 46 days, increased representation of patients and healthcare professionals at the CHMP and Pharmacovigilance Risk Assessment Committee, and a more joined-up approach to decision-making and information sharing between the EMA and member state agencies.⁹⁶

93 As set out in the European Commission's proposed reforms to the EU pharmaceutical legislation. Available at: https://eur-lex.europa.eu/resource.html?uri=cellar:e3f40e76-e437-11ed-a05c-01aa75ed71a1.0001.02/DOC_1&format=PDF [accessed April 2024]

94 EFPIA (2022) Addressing patient access inequalities in Europe. Available at: <https://www.efpia.eu/media/677156/addressing-patient-access-inequalities-in-europe.pdf> [accessed April 2024]

95 Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and The Committee of the Regions, Pharmaceutical Strategy for Europe COM/2020/761 final

96 European Commission (2023) Proposal for a regulation of the European Parliament and of the Council laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006.

Further, a number of provisions in the proposal have been made with the aim of ensuring that Europe's regulatory framework is future proof; that is, it will be able to deal with emerging developments in science. These provisions include ones related to adapted clinical trials, use of real-world evidence, secondary use of health data, and regulatory sandboxes. A regulatory sandbox could provide the opportunity to advance regulation through proactive regulatory learning and support regulators with developing better knowledge to find the best means to regulate new innovations, particularly for disruptive technologies or instances of high uncertainty.

However, progress on regulatory efficiency could be undone by misguided policies that link regulatory incentives to evidence development. For example, amendments to the European Commission's proposals that were recently voted on by the European Parliament include provisions to incentivise the use of comparative clinical trials through the granting of 12 additional months of RDP.⁹⁷ This could have unintended consequences for early initiation or discontinuation of research projects, clinical development times, the location of clinical trials, timelines for the submission of marketing authorisation applications, and incentives for innovation overall and in different therapy areas.

Proposals that aim to increase transparency of information regarding placing centrally approved products on the market

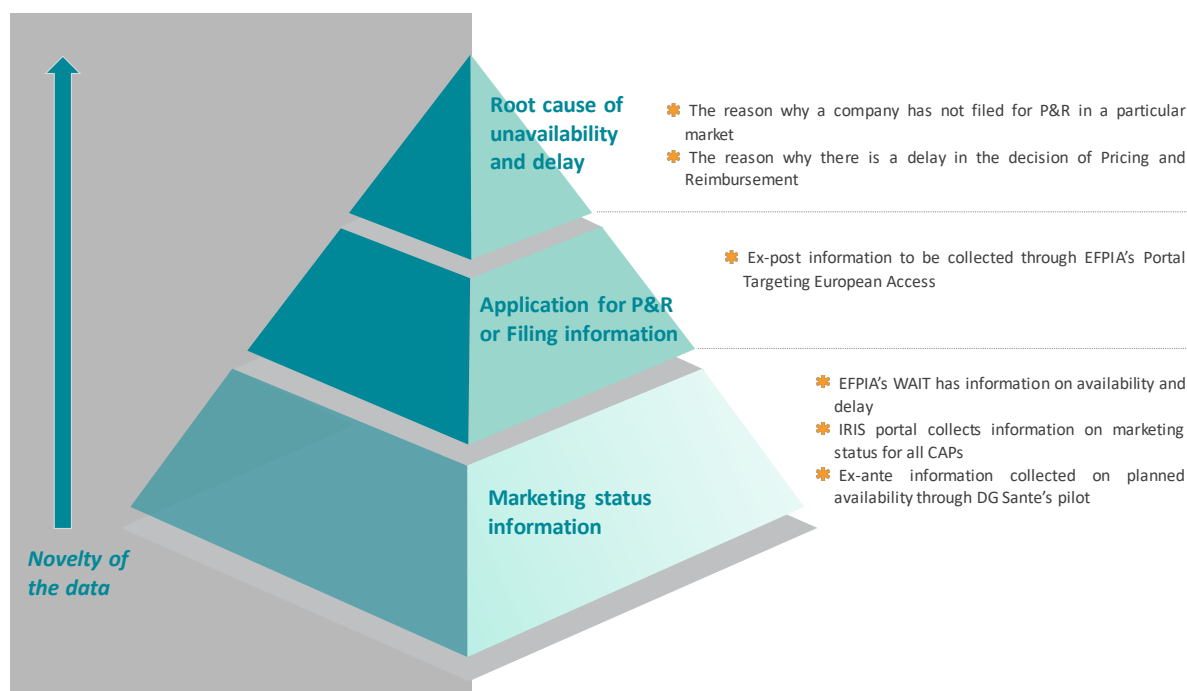
The industry has launched a European Access Hurdles Portal where marketing authorisation holders (MAH) can provide timely information regarding the timing and processing of pricing and reimbursement (P&R) applications in 30 European countries, including the reasons for a delay in the P&R decision or the MAH having not filed in a particular market.

EFPIA already contributes to transparency on unavailability and delay with its yearly published Patient W.A.I.T. report highlighting the delays to patient access across the EU as well as the present report on the 10 most common root causes of unavailability and access delays. However, to better understand the root causes and monitor how they evolve, the industry has launched a European Access Hurdles Portal.

Marketing authorisation holders of centrally approved products are requested to provide timely information regarding the timing and processing of P&R applications in the 30 European countries, including the reasons for delay in the P&R decision or the MAH having not filed for P&R in a particular market.

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European Parliament legislative resolution of 10 April 2024 on the proposal for a directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC (COM(2023)0192 – C9-0143/2023 – 2023/0132(COD))

Figure 23: New information on unavailability and delay

Source: EFPIA

Initial results from the portal were first published in April 2023 based on data collected on 32 products.⁹⁸ They showed for the first time the percentage of products that have been filed for P&R or reimbursed following marketing authorization and showed that even including products that have only recently been approved, the majority have already been filed or reimbursed. The portal also allows us to understand the reasons for delay by quantifying the prevalence of the root causes described above.

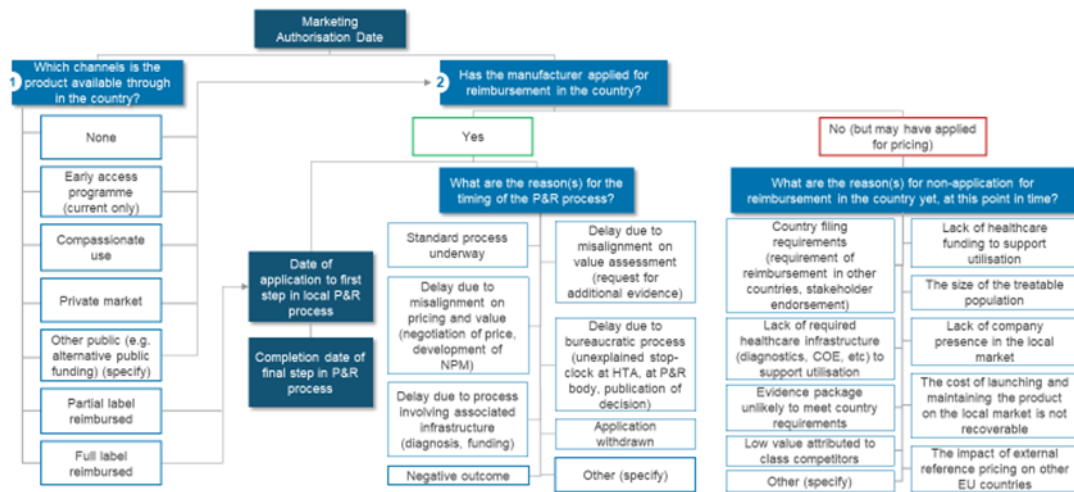
The second review of results from the portal is being published separately in June 2024 and includes aggregate data collected on the timing of filing and root causes of delays in filing for different products. With the portal now in its second year of operation, 100% of EFPIA members with products eligible for inclusion in the portal submitted data, providing information on 66 products. The most recent results support that the causes of unavailability and delay are multifactorial and document that it is a shared responsibility requiring a shared solution.

The data from the portal will only become richer over time, allowing us to both monitor and understand in greater detail the reasons for unavailability. Through regular reports, it will also be possible to track progress in lowering the hurdles that cause unavailability and delay.

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CRA, EFPIA (2023) European Access Hurdles Portal: initial results. Available at: <https://www.efpia.eu/media/677291/european-access-hurdles-portal-efpia-cra-report-200423-final.pdf> [accessed April 2024]

Figure 24: Data captured by the portal



Proposals to facilitate a process that allows prices to align with value and ability to pay

The industry is committed to supporting the development of **novel pricing and payment models**. When used appropriately and tailored to the situation, they can accelerate patient access, allowing payers to manage clinical uncertainty, budget impact, and sustainability of the healthcare system, while providing sufficient incentives for innovation.^{99,100}

Although some novel pricing and payment models are being used today, legal barriers, a lack of appropriate data infrastructure, and an unwillingness to adapt current systems often prevent their use. To help address these barriers, the industry proposes a set of guiding principles regarding the use of novel pricing and payment models:

1. **Access Principle:** Novel pricing and payment models should facilitate broad and timely patient access while balancing the sustainability of the healthcare system and incentives for innovation.
2. **Value Principle:** A high-quality, methodologically robust and mutually agreed value-based framework is the foundation for novel pricing and payment models.
3. **Collaboration Principle:** Payers and companies should work together to anticipate where novel pricing and payment models are needed and ensure they are fit for purpose.
4. **Transparency Principle:** There should be transparency regarding the existence of the novel pricing and payment agreements and the outcomes data generated (with appropriate safeguards in place), the confidentiality of commercial terms being maintained.

99 <https://efpia.eu/media/554543/novel-pricing-and-payment-models-new-solutions-to-improve-patient-access-300630.pdf>

100 <https://www.efpia.eu/media/602581/principles-on-the-transparency-of-evidencefrom-novel-pricing-and-payment-models.pdf>

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5. **Infrastructure Principle:** Stakeholders should work together to ensure that the required data infrastructure is fit for purpose and that legal frameworks are in place to enable access.

The industry has an important role to play and should commit to an open dialogue and collaboration with payers and policymakers to reach a win-win solution that puts patients' interests first.

Proposals to improve the efficiency and quality of value assessment

The industry is committed to contributing to the creation of an **efficient system of European assessments of relative efficacy at time of launch** in the context of the implementation of the HTA Regulation.

HTA agencies currently reach different conclusions on the medical impact (relative efficacy and/or relative effectiveness assessment) of new pharmaceuticals, even though the data studied—such as safety and efficacy data from registration trials—is predominantly the same for all markets. This occurs because HTA agencies adopt different approaches to rating and interpreting the data; they might apply to trial design, relevant endpoints, appropriateness of defined patient subgroups, and treatment comparators. With the establishment of the legal basis of the EU HTA regulation and the beginning of the implementation period (from January 12, 2025, the regulation will apply to oncology and ATMP products, followed by orphan medicinal products three years later and all other centrally approved medicines after five years), an opportunity exists to establish an efficient system of European assessments of relative efficacy at time of launch. However, the EU HTA regulation will deliver against its promise only if all stakeholders collaborate during the coming years on implementing a future-proof system that delivers high-quality outputs that are relevant for decision-making in member states.

For example, it is important to avoid a scenario under which implementation of the EU HTA regulation leads to a delay in national processes. Member states may opt to wait for the JCA report before beginning their national P&R process. To realise the goal of faster patient access to new medicines, it is important that member states continue to initiate national P&R processes in a timely manner. Where a risk of delays exists, opportunities for national HTA agencies to accelerate the national clinical assessment by leveraging the JCA report should be used to minimize delays to the overall access timelines.

Proposals to ensure equity of access and solidarity across EU member states

The industry is committed to participating in a **structured dialogue on a conceptual framework for equity-based tiered pricing (EBTP)**. The objective—anchored in a principle of solidarity among countries—is to ensure that ability to pay across countries is considered in the prices of innovative medicines to reduce unavailability of new medicines and access delays.

Building on value-based pricing as the foundation for pricing innovative medicines (with the pricing of medicines being based on the value they deliver to patients, healthcare systems, and society), EBTP is a framework for the pricing of medicines that takes into account a country's ability to pay with the objective of improving patient access (defined broadly in terms of speed and availability) across Europe. The commitment of both member states and industry is needed for EBTP to work in practice, and some of the current barriers to access and differential pricing must also be addressed, including the use of external

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reference pricing and extraterritoriality. EFPIA members support an EBTP approach based on a concrete conceptual framework¹⁰¹ with the following characteristics:

- To promote faster and greater access, companies would voluntarily commit to applying EBTP principles to specific innovative medicines.
 - The framework would include simple rules regarding the tiers and how EBTP affects the price of medicines but would leave room for individual companies to determine how it is applied.
- For prices to reflect value and be consistent with EBTP, companies will continue to negotiate with individual countries so that prices will reflect the value that medicines deliver in that market. EBTP would set a framework for prices, but the final price would depend on company strategy and negotiations in the member states. EBTP does not replace value assessment or value-based pricing.
- The resulting price must be commercially confidential. Given the need for price confidentiality, it will not be possible to publicly observe exactly how EBTP is working in practice. A process of verification would be required.

The proposed industry commitments would be contingent on the implementation of corresponding commitments from other parties necessary for the EBTP framework to achieve the intended impact.

1.9. Conclusion

The need for a dialogue on how to improve availability and reduce delays is clear. Although availability will inevitably vary to some extent across European markets, patients in one part of Europe should not have to wait over 800 days longer for a new medicine than those in another part. Patients living with one condition in a country should not have to wait longer than patients living with a different condition. We need to work together to ensure that access to medicines is based on the patient's clinical need, not their postcode. The industry has made a number of commitments demonstrating how it can play a key role in addressing unavailability and delay.

101

<https://efpia.eu/media/636825/a-shared-approach-to-supporting-equity-based-tiered-pricing.pdf>

Glossary:

- **Access:** Refers to actual systematic usage of medicines.
- **Availability:** Inclusion of a centrally approved medicine on the public reimbursement list in a country. A medicine is available on the market if patients can receive the medicine under a reimbursement scheme. The availability date is the first date when doctors can prescribe or hospitals can administer the medicine to patients in the country, who will be able to benefit from reimbursement conditions applicable in the country (i.e., administrative procedures required for inclusion in the positive reimbursement list have been completed, where applicable).
- **Time to availability:** The time to availability is the number of days between EMA marketing authorisation and the date of availability.
- **Market launch:** This refers to a product being placed on the market for sale (not to it being by national or regional authorities).