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

Executive summary[1]

The unprecedented speed of innovation exhibited over the last five years and the promise of the industry pipeline[2] 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 2025 Survey, the average time to reimbursement for innovative treatments across EU27 countries has reached 597 days, ranging from 158 days in Germany to 1,110 days in Romania. The median time to availability is 532 days, with even more pronounced disparities between countries - ranging from 56 days in Germany to 1,201 days in Romania.[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 the proposed Biotech Act and whether it will improve access to medicines for patients in the EU.

Over the past six 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.

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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) 2024 Pipeline Review – Innovation for Unmet Need. Available at: https://efpia.eu/media/mezjxddv/2024-pipeline-review.pdf [Accessed April 2026]

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 2025 Survey.

5 EFPIA (2020) The root causes of unavailability and delay to innovative medicines. Available at: https://www.efpia.eu/publications/downloads/efpia/the-root-causes-of-unavailability-and-delay-to-innovative-medicines/ Accessed April 2026]

This year we include two additional sections, one on root causes of unavailability and delay in smaller European markets (where smaller markets are defined as those with a population of less than 4 million and lower levels of filing)[6] and an additional analysis on regulatory approval assessments in the EU and comparator countries to monitor the potential impact of the US Most Favoured Nation (MFN) drug pricing policy on the availability of, and delays in access to, new molecules across global markets.

Table 1: The root causes of delays and unavailability

Category	Potential root causes
The time before marketing authorisation	1. The speed of the regulatory process 2. Accessibility of medicines before marketing authorisation
The pricing and reimbursement process	3. Initiation of the process 4. The speed of national timelines and adherence
The value assessment process	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	8. Insufficient budget to implement decisions 9. Diagnosis, supporting infrastructure, and relevance to patients
The subnational approval process	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 is committed to working with the European Commission to achieve these shared goals and ensure patients across Europe have reliable access to life-saving medicines. This requires targeted, evidence-based policy solutions. The industry supports the European Commission's ambition to ensure timely access to critical medicines through the Critical Medicines Act and the proposed Biotech Act.

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:

6 This draws on the analysis developed in the CRA Root causes of unavailability and delay in smaller markets report, May 2025

- **Working together 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. 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. The proposed Biotech Act could also improve the clinical trial environment, if appropriately designed and implemented. Accelerating the regulatory approval timeline is even more important given the potential impact from MFN.
- **The creation of a portal where marketing authorisation holders (MAHs) can provide timely information regarding the timing and processing of pricing and reimbursement (P&R) applications in the 30 European countries. The portal builds on the industry's commitment to submit P&R applications in all EU Member States no later than two years after EU market authorisation, provided that local systems permit this.** 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 fifth year of operation, and EFPIA has published four reports documenting the novel information collected in the portal and its relevance to the debate on medicine availability.[7] This information will be particularly important given the forthcoming implementation of the provisions contained in the revised EU pharmaceutical legislation (specifically Article 56a of the Directive and Article 5a of the Regulation) aiming at making available centrally approved products on member States' markets. This will also be important in observing the potential impact of the MFN on access to medicines in Europe.
- **A conceptual framework for equity-based tiered pricing (EBTP) and ensuring availability to innovation as soon as possible** 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. This framework includes the ability to launch medicines in the private market immediately after regulatory approval, establish a public list price and ensure access is provided for patients prior to the completion of pricing and reimbursement process.
- **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

7 CRA, EFPIA (2025) European Access Hurdles Portal: Results from the third year of data collection. Available at: https://www.efpia.eu/media/lrbdpuoz/cra-efpia-european-access-hurdles-portal-2025.pdf [Accessed April 2026].

providing sufficient incentives for innovation.[8,9] This is also an important mechanism that can be used, instead of arbitrary clawbacks to help provide budget certainty. They can also be used in association with an increase in European health spending, to ensure spending is focused on areas delivering value to patients and the healthcare system. However, they need to negotiated in a fashion that ensure compliance with Transparency Directive.

- Contributions to the achievement of an **efficient system of European assessments of relative efficacy at time of launch** in the context of the Health Technology Assessment Regulation (HTAR) ensuring that this accelerates access to medicines in Europe and does not introduce an additional barrier. This is more important given the context of the MFN.

The present report is the seventh 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.[10]

The importance of addressing unavailability and delays was highlighted in the European Commission's General Pharmaceutical Legislation in Europe.[11] The subsequent debate in the European Parliament has reflected this (see Box 1).

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8 EFPIA (2020, July) Addressing Healthcare Challenges. Novel Pricing and Payment Models: New solutions to improve patient access. Available at https://efpia.eu/media/554543/novel-pricing-and-payment-models-new-solutions-to-improve-patient-access-300630.pdf [Accessed April 2026]

9 EFPIA (2021, April) Addressing Healthcare Challenges. Principles on the Transparency of Evidence from Novel Pricing and Payment Models. Available at https://www.efpia.eu/media/602581/principles-on-the-transparency-of-evidencefrom-novel-pricing-and-payment-models.pdf [Accessed April 2026]

10 EFPIA (2019) How long should you WAIT for a new medicine? Europe's post code lottery. Available at 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/ [Accessed April 2026]

11 European Medicines Agency (2025) Reform of the EU pharmaceutical legislation. Available at: https://www.ema.europa.eu/en/about-us/what-we-do/reform-eu-pharmaceutical-legislation [Accessed April 2026]

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

Source: European Parliament, European Parliament legislative resolution of 10 April 2024[12]

> *". . . 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."*

Prior to the political agreement on the reform of the EU pharmaceutical legislation in December 2025, the EPSCO Council agreed on the general approach on the proposed Critical Medicines Act (CMA), a regulation aimed at improving the availability, supply and production of critical medicines within the EU.[13,14] The draft CMA proposal includes strengthened collaborative procurement options to improve availability of medicines in certain circumstances. This shares elements of a proposal from the EPSCO Council in December 2024, calling for voluntary cooperation on joint procurement of medicinal products between Member States facing similar challenges in terms of availability and accessibility of innovative medicinal products.[15] However, while these options may be appropriate under very specific circumstances where they accelerate patient access to critical medicines, a systematic application could create more harm than offering a more permanent solution to access related issues.[16]

On 16 December 2025 the European Commission also published a proposal for a Biotech Act. Although focused primarily on the innovative eco-system, this recognises that a conducive environment for clinical trials is essential to speed-up market access for novel medicines, and the need to address regulatory fragmentations across Member States that

12 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))

13 European Commission (2025) Critical Medicines Act. Available at: https://health.ec.europa.eu/medicinal-products/legal-framework-governing-medicinal-products-human-use-eu/critical-medicines-act_en [Accessed April 2026]

14 European Council (2025, December 2) Critical medicines act: Council agrees its position on new rules to tackle shortages. Available at: Critical medicines act: Council agrees its position on new rules to tackle shortages [Accessed April 2026]

15 EPSCO (2024) Proposal for Voluntary Cooperation of Member States on Joint Procurement of Medicinal Products. Available at: https://data.consilium.europa.eu/doc/document/ST-15379-2024-REV-1/en/pdf [Accessed April 2026]

16 EFPIA (2025) EFPIA response to the Critical Medicines Act. Available at: https://efpia.eu/news-events/the-efpia-view/statements-press-releases/efpia-response-to-the-critical-medicines-act/ [Accessed April 2026]

limit the system's efficiency underlying the need address slow and complex regulatory frameworks.[17]

The industry shares the existing 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. It also recognises that the challenge associated to ensuring availability of innovative medicines access Europe are likely to be exacerbated by geopolitical policy trends (although it is too early to observe systematically in data to date).[18,19,20]

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):

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

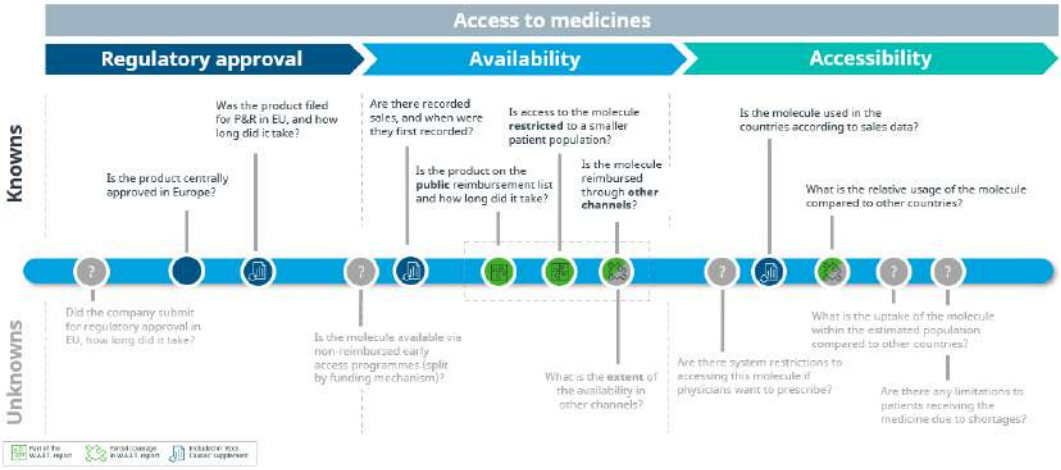
17 European Commission (2025) Proposal for a Regulation to establish measures to strengthen the Union's biotechnology and biomanufacturing sectors (European Biotech Act). Available at https://health.ec.europa.eu/publications/proposal-regulation-establish-measures-strengthen-unions-biotechnology-and-biomanufacturing-sectors_en [Accessed April 2026]

18 Reuters (2026) Drugmakers delay some European launches with a wary eye on Trump's pricing policies. Available at https://www.reuters.com/business/healthcare-pharmaceuticals/drugmakers-delay-some-european-launches-with-wary-eye-trumps-pricing-policies-2026-03-31/ [Accessed April 2026]

19 Pharmaceutical Technology (2026) The Most Favored Nation Policy: early insights into Europe's response. Available at https://www.pharmaceutical-technology.com/analyst-comment/most-favored-nation-policy-early-insights-into-europe-response/?cf-view [Accessed April 2026]

20 Copenhagen Economics (2026) Economic contribution of EUCOPE's membership and trade implications following U.S. policy measures: EUCOPE's membership survey. Available at https://copenhageneconomics.com/wp-content/uploads/2026/01/EUCOPE_economic-contribution-and-trade-implications.pdf [Accessed April 2026]

Figure 1: Components involved in assessing access to medicines

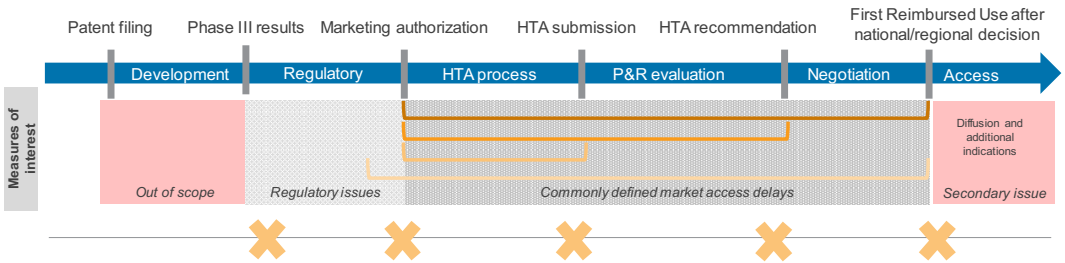


Source: IQVIA (2026)

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

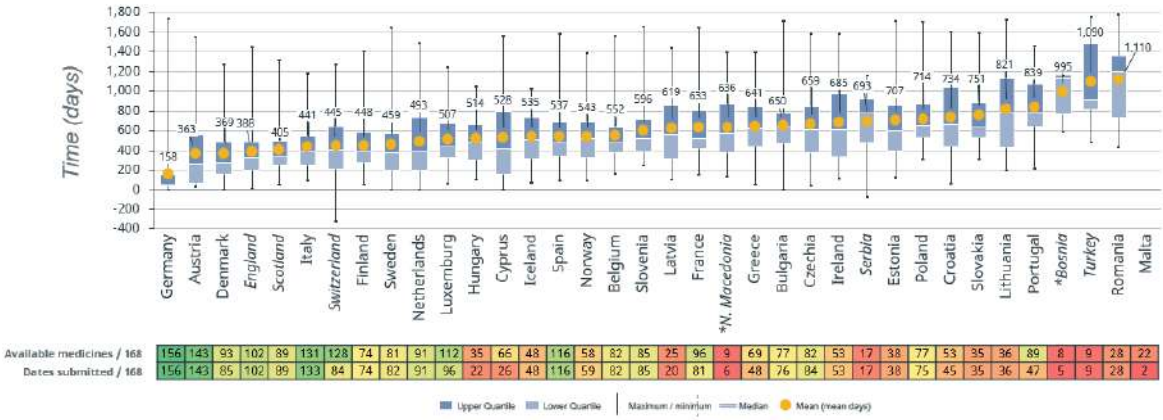


Source: EFPIA

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 2025 survey (in Figure 3 below), the average time to reimbursement from central approval by the EMA for innovative treatments across the EU and European Economic Area countries ranges from 158 days in Germany to as long as 1,110 days in Romania; the average is 597 days. The median time to availability is 532 days, with even more pronounced disparities between countries - ranging from 56 days in Germany to 1,201 days in Romania.

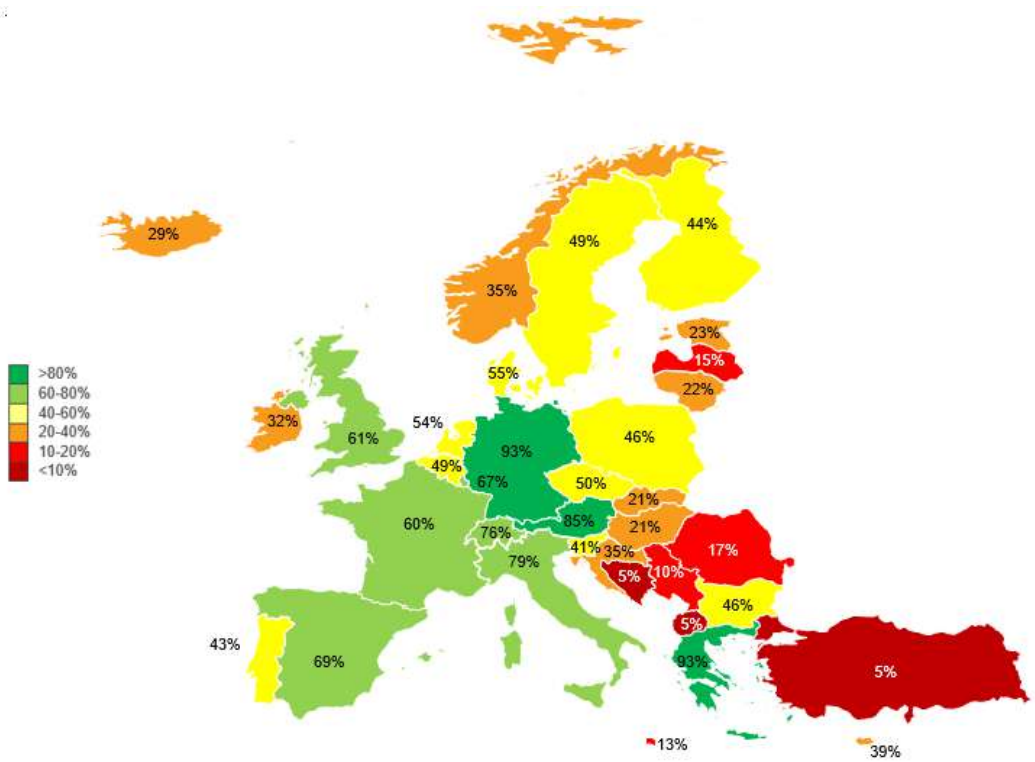
Figure 3: Mean time to availability in days (2021–2024)



Source: The Patient W.A.I.T. Indicator 2025 Survey

Patients in certain European countries can wait about seven times longer than patients in other countries to get access to the same medicine, from as little as five months to 37 months. Referring to median times, patient access disparities range from 2 months to 40 months. Some common patterns are evident: typically, patients in Northern and Western Europe get access to new treatments between 100 and 500 days after market authorisation has been granted, whereas patients in Southern and Eastern Europe wait between 500 and 900 days. This means that at any time, availability of medicines varies dramatically across Europe (as shown in Figure 4 below).

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

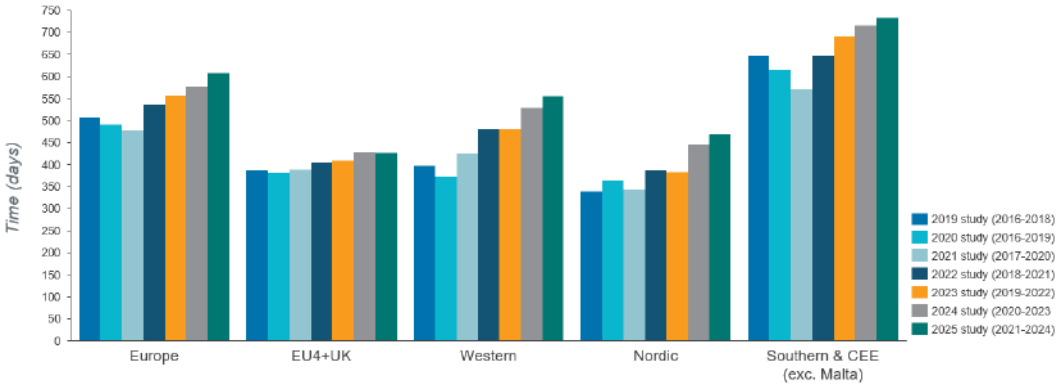


Source: The Patient W.A.I.T. Indicator 2025 Survey.

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 sixth 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).[21] 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 in the EU has slightly increased to 952 days between the fastest (Germany) and slowest (Romania) countries in Europe.

There is also evidence to suggest that, across Europe, delays in availability of innovative medicines are not getting any better and, in most regions, may even be gradually lengthening over time (see Figure 5). This is most obvious in Western European countries and the Nordics, but it is clear that all regions have seen an increased delay in time to availability of innovative medicines in the most recent W.A.I.T. data, with the EU average time to availability increasing by 19 days from 578 days in the 2024 study to 597 days now.[22]

Figure 5: Comparison of delay over time (mean delays in days), by region[23]



Source: The Patient W.A.I.T. Indicator 2025 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). While the trend is roughly similar across recent years, there has been a small decrease in availability throughout Europe in 2025. This decrease is evident all countries. Overall, unavailability has increased slightly since 2019, from 46% to 49%. The W.A.I.T. data also indicate that the proportion of available products facing restrictions (compared to full availability) is increasing over time, perhaps indicating a growth in the use of alternative routes to achieve availability. In 2019, the rate of full availability was 42%, while in 2025 this is now reduced to 28% across Europe, with the share of medicines fully

21 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 2026]

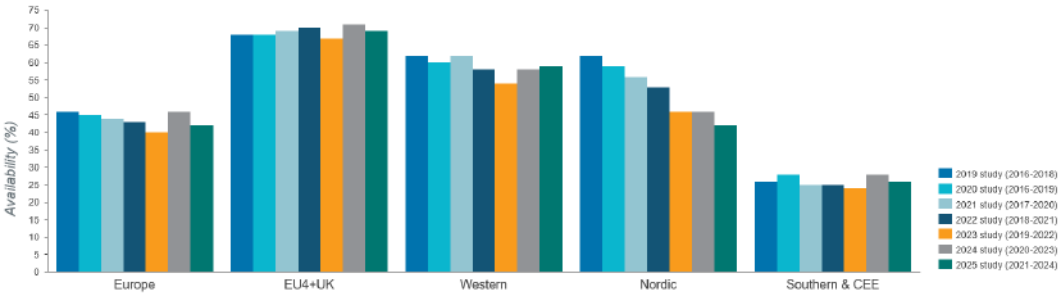
22 The countries were grouped by geography: **EU4+UK:** England, France, Germany, Italy, Scotland, Spain; **Western:** Austria, Belgium, Ireland, Luxembourg, Netherlands, Portugal, Switzerland; **Nordic:** Denmark, Finland, Iceland, Norway, Sweden; **Southern and Central and Eastern European (CEE):**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

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

available on public reimbursement having declined substantially and nearly one fifth of medicines now available under restricted conditions.

Although the rate of availability of innovative medicines is still lowest in Southern and CEE countries, rates there have changed only minimally over time. Given the nature of the W.A.I.T. analysis with a changing cohort over time, it is too early to determine if this is a change in the trend or natural variation. This concept is explored below.

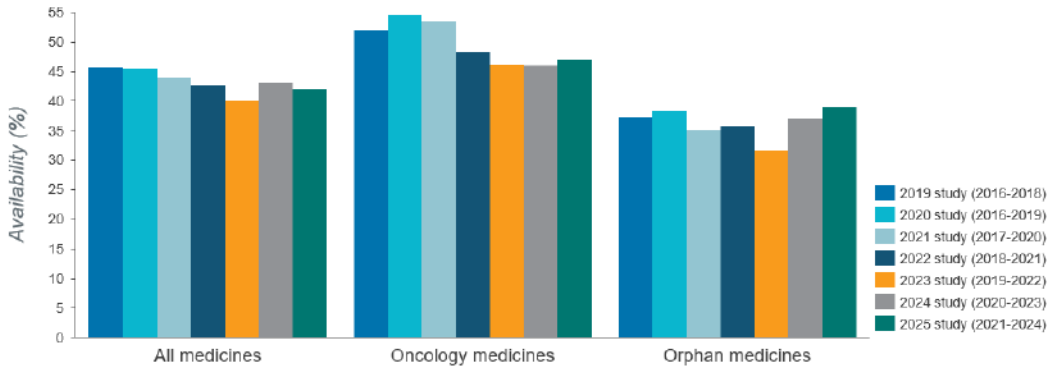
Figure 6: Comparison of rate of availability over time (mean availability in percentage), by region



Source: The Patient W.A.I.T. Indicator 2025 Survey

Also, observable are developing 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 generally decreased over time. While oncology medicines continue to have a higher rate of availability to “all medicines” the time to availability has also increased to 655 days, compared to 586 days in 2024. For orphan medicines, the rate of availability remains consistently lower; however, after a more significant decrease in 2023, there has been an increase in the rate of availability in the W.A.I.T data for subsequent years (2024, 2025) compared to previous levels. Availability of orphan medicines continues to vary considerably across Europe, with longer delays and lower availability observed in CEE and Southern European countries.

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

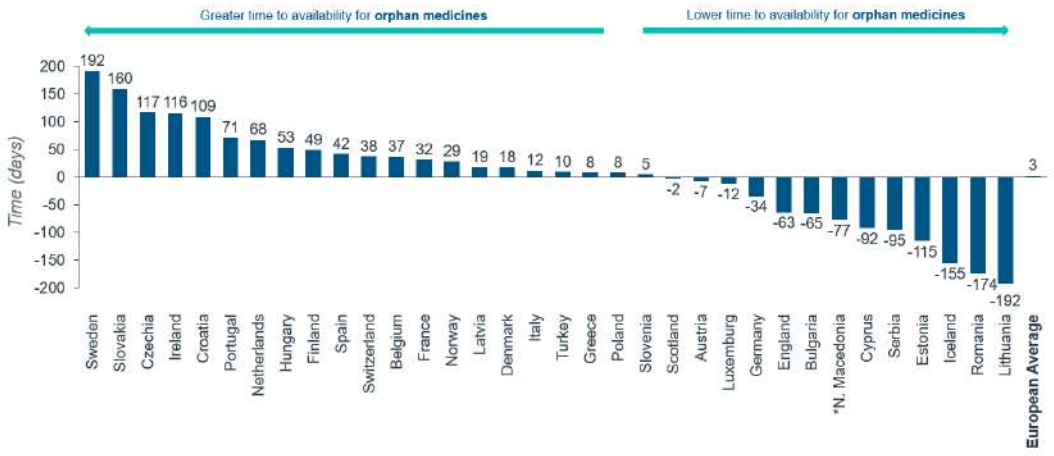


Source: The Patient W.A.I.T. Indicator 2025 Survey

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 (2021–2024)



Source: The Patient W.A.I.T. Indicator 2025 Survey; based on local times to availability. Note: Positive values mean orphan drugs are slower than all medicines by the indicated number of days. Malta and Bosnia are excluded because there is no data on orphan medicines available.

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 2023 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.[24]

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 Greece, the shortest delay to oncology medicines was 54 days and the longest 1400 days; in Scotland, the variance was 0 days to 1,230 days; in Czechia, 42 days to 1,589 days.[25]

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.[26]

24 Hofmarcher, T., Szilagyiova, 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

25 The Patient W.A.I.T. Indicator 2025 Survey

26 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]

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).[27] 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).

Table 2: The root causes of unavailability and delay

Category	Potential root causes
The time before marketing authorisation	1. The speed of the regulatory process 2. Accessibility of medicines before marketing authorisation
The pricing and reimbursement process	3. Initiation of the process 4. The speed of national timelines and adherence
The value assessment process	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	8. Insufficient budget to implement decisions 9. Diagnosis, supporting infrastructure, and relevance to patients
The subnational approval process	10. Multilayer decision-making process

Source: EFPIA

27 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.

We now turn to the evidence of what causes unavailability. As set out in an 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."[28]

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.

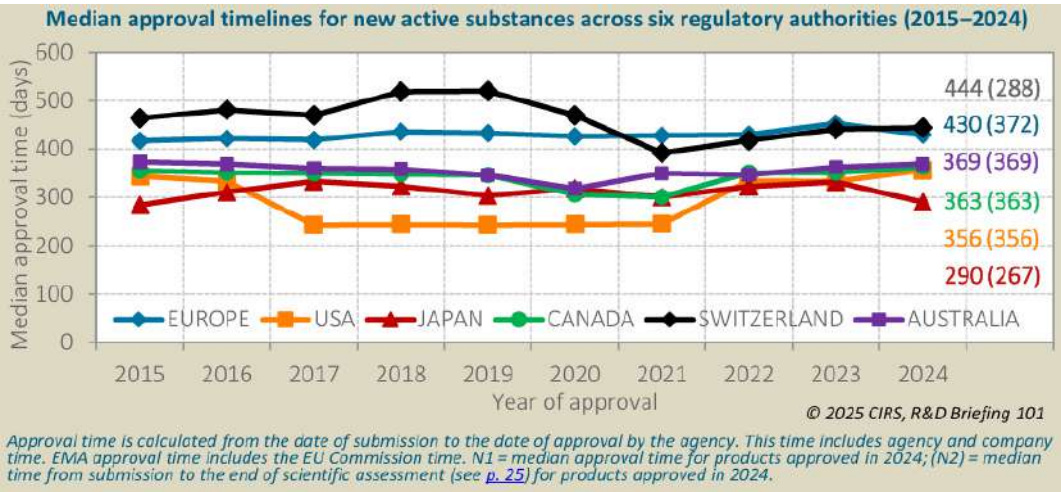
The speed of the regulatory process

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 than some international processes, particularly that of the United States (Figure 9 below).[29] From the international comparisons shown in Figure 9, it appears that the approval timelines have generally converged in other regions of the world (with the exception of the most recent observation for Japan), whereas times in Europe have remained relatively unchanged; hence, Europe is lagging behind.

28 OECD (2020, April) Addressing Challenges in Access to Oncology Medicines, Analytical Report. Available at: https://www.oecd.org/content/dam/oecd/en/publications/reports/2020/04/addressing-challenges-in-access-to-oncology-medicines_5f0e2f62/699520d0-en.pdf [Accessed April 2026]

29 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.

Figure 9: Comparison of the length of time of market authorisation processes



Source: CIRS (2026)[30]

The US also approves a higher number of new medicines relative to Europe. Looking at all 56 new active substances (NAS) approved in the US, EU or Japan in 2024, analysis finds that the US has the highest approval rate at 100% (56 NAS), 79% of which were approved on the first review, and the EU lags behind at 61% (34 NAS).[31] Between 2021 and 2025, Europe's share of yearly FDA approvals has fallen from 65% to 36%.[32]

New evidence shows that that the number of products approved in the US and absent from Europe is growing. Among 526 medicines approved by the US FDA from 2016 to 2025, 175 (33%) lack approval in Germany and 193 (37%) lack EMA approval.[33]

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.

- One study focusing on 16 tyrosine kinase inhibitors approved by the US Food and Drug Administration (FDA) between 2001 and 2012 found that while the average time spent on review and approval in the 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). Authors also found that companies filed for market authorisation in both

30 CIRS (2026) New drug approvals in six major authorities 2015-2024: Changing regulatory landscape and facilitated regulatory pathways. Available at: https://cirsci.org/wp-content/uploads/dlm_uploads/2025/08/CIRS-RD-Briefing-101-v1.1.pdf [Accessed April 2026]

31 IQVIA (2024) Assessing Availability of New Drugs in Europe, Japan, and the U.S. Available at: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/assessing-availability-of-new-drugs-in-europe-japan-and-the-us [Accessed April 2026]

32 The analysis tracks whether NAS approved by the FDA in any given year subsequently receive approval in other countries. Thus, earlier cohorts are likely to show higher percentages as they will have been on the market for longer.

33 CRA (2026) Europe's pharmaceutical innovation gap: An assessment of missing and delayed regulatory approvals compared with the US and China (2016–2025) and implications for Germany. A report for the vFA.

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.[34]

- 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).[35]
- The latest evidence suggests that these trends remain unchanged: a 2025 study reviewed 152 novel oncology therapies approved by both the FDA and the EMA between January 2003 and December 2024 and found that 94% were approved by the FDA before the EMA.[36] This was found to be primarily attributable to differences in review time, with the median review time at the EMA (422 days) extending significantly beyond the FDA median review time (207 days). Most therapies were first filed in the US; of the 36 therapies that were first filed with the EMA, 30 of these (83%) were still approved first by the FDA.

For other categories of medicines, the difference may be smaller, but the FDA is still faster than the EMA.[37]

Many of 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). 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.

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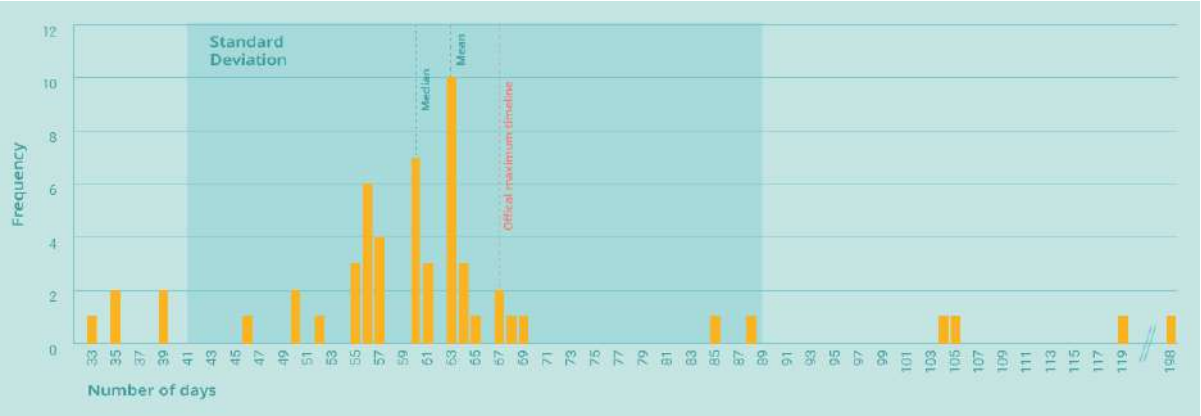
34 Shah, R. R., Roberts, S. A. and Shah, D. R. (2013) A fresh perspective on comparing the FDA and the CHMP/EMA: approval of antineoplastic tyrosine kinase inhibitors. *British Journal of Clinical Pharmacology* 76(3): 396–411

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

36 Friends of Cancer Research (2025) Available at: https://friendsofcancerresearch.org/blog/20-years-of-fda-leadership-in-novel-cancer-drug-approvals/ [Accessed April 2026]

37 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



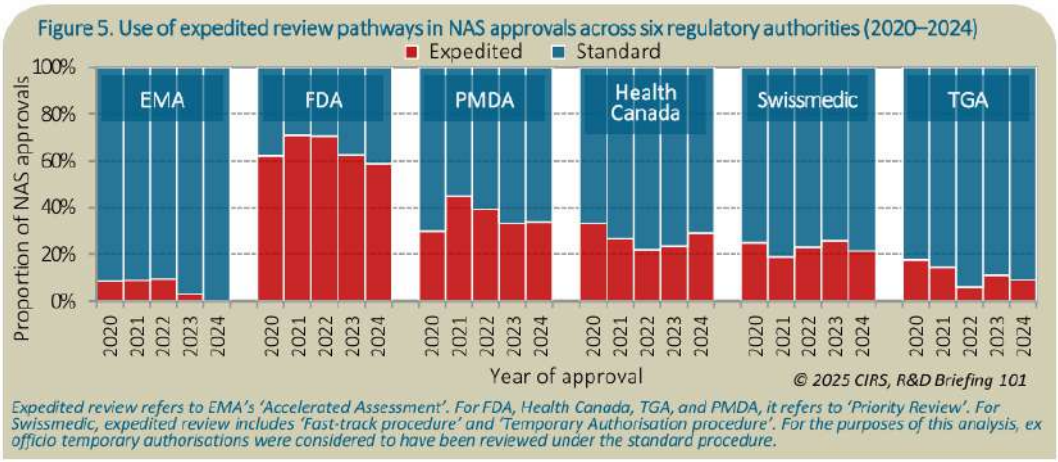
Source: Vintura (2021).[38] Timelines reflect oncology therapies (new molecular entities only) evaluated by the CHMP between 2016 and 2020.

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 2025, no new medicine approved by the EMA went through the accelerated assessment procedure. This is significantly lower than use of equivalent expedited review pathways by the PMDA (34%) and FDA (59%). This is lower than previous CIRS reports and reflects lower successful use of accelerated channels. The lower successful use of expedited reviews in Europe is attributed in part to the EMA's ability to revert to a standard review timeline if the accelerated timeline cannot be met (as occurred for one medicine) and in part to denial of requests for accelerated review (as occurred for two medicines).[39]

38 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 April 2026]

39 CIRS (2026) New drug approvals in six major authorities 2015-2024: Changing regulatory landscape and facilitated regulatory pathways. Available at: https://cirsci.org/wp-content/uploads/dlm_uploads/2025/08/CIRS-RD-Briefing-101-v1.1.pdf [Accessed April 2026]

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



Source: CIRS (2026)[40]

Even with the European Commission's proposals to streamline the EU's regulatory procedures, evidence suggests that Europe is lagging behind in terms of of the speed of regulatory approval and that this is unlikely to catch-up in the near future (Figure 9). So even though the problem has been recognised, it remains true that 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.[41,42] 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.[43]

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. For example, in France, products with high unmet need can be granted an "autorisation

40 CIRS (2026) New drug approvals in six major authorities 2015-2024: Changing regulatory landscape and facilitated regulatory pathways. Available at: https://cirsci.org/wp-content/uploads/dlm_uploads/2025/08/CIRS-RD-Briefing-101-v1.1.pdf [Accessed April 2026]

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

42 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.

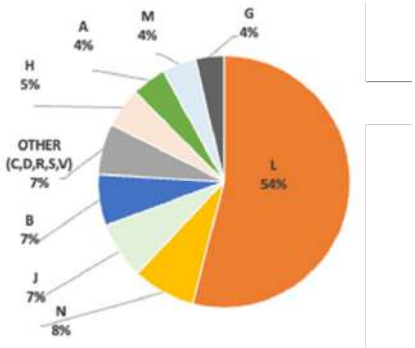
43 In addition, most countries have named patient compassionate-use programs that might be offered to patients with life-threatening or seriously debilitating conditions or an area of unmet clinical need. These have recently been documented in Access to medicines in Europe: Delays and challenges for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

d'accès précoce" (AAP)[44] 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.

Somewhat comparable schemes have also been developed in other markets. An example is England's "early access to medicines scheme" (EAMS), launched in 2014. 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).[45]

In Italy, the 648 List enables reimbursed access to new medicines before their marketing authorisation, and access is continued until the completion of the P&R process. The initial intent of the programme was to provide off-label access to medicines in cases of high unmet need; its role has extended gradually over time to function also as an early access programme for medicines under development.[46] A recent analysis has shown that the type of medicines that are most commonly accessible through the 648 List are cancer drugs (ATC L – 54% of total medicines), followed by CNS drugs (ATC N – 8% of total medicines) (Figure 12). Notably, most of the medicines included in the list are for off-label use rather than for supporting access prior to marketing authorisation.

Figure 12: ATC class distribution of products in Italy's 648 List[47]



Source: Tarantola, A. et al. (2024)

44 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.

45 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 [Accessed April 2026]

46 Tarantola, A. et al. (2024) Early access programs for medicines: comparative analysis among France, Italy, Spain, and UK and focus on the Italian case. *Journal of Pharmaceutical Policy and Practice*. 16(1)

47 Tarantola, A. et al. (2024) Early access programs for medicines: comparative analysis among France, Italy, Spain, and UK and focus on the Italian case. *Journal of Pharmaceutical Policy and Practice*. 16(1)

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.[48] For example, in Germany, the standard process gives manufacturers a temporary period of value-based 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 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.[49]
- In Greece, a product can be filed for reimbursement only if it is reimbursed in five of 11 specified countries.[50]

In other cases, there are no formal rules that dictate when a product can be filed, but there is an informal preference for filing only after there are sufficient HTA reports or

48 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.

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

50 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.

reimbursement decisions from other countries. There is often a preference for English language reports; hence, countries may wait for England's NICE, Scotland's SMC, or Ireland's NCPE to publish their assessments before conducting a local evaluation.

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.[51] 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.[52] 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.[53] 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.[54,55]

The timing of the HTA process in different countries has not been documented in many studies and is changing due to the introduction of joint clinical assessment. Illustrative timelines for the HTA process in various European countries are shown in Figure 13 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*.

51 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

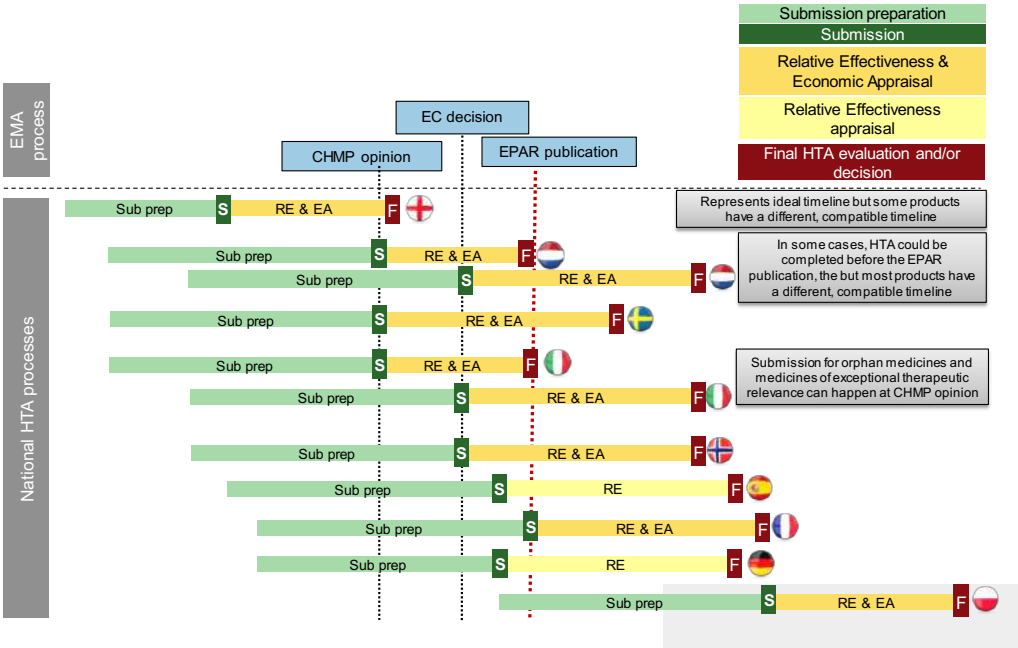
52 Riigi Teataja (2022). Health Insurance Act. Available at https://www.riigiteataja.ee/en/eli/520012014001/consolide [Accessed April 2026]

53 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

54 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 [Accessed April 2026]

55 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 13: 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 literature shows 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.[56,57]
- 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, resource capacity means that some countries are prioritised over others. 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 14 supports this finding by demonstrating that products manufactured by larger companies generally are more available. With the phased implementation of joint clinical assessment in Europe, there may be efficiencies

56 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

57 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

gained from use of the EU clinical dossier at a national level. However, the need to prepare an additional EU dossier on top of all national HTA dossiers will require more company resources.

Figure 14: Percentage of products available in EU countries, segmented by company size

Sorted by total availability (%) according to EFPIA W.A.I.T. (2021-2024 cohort)

Country	Top-20 global pharma	Other biotech and SME companies	Large company delta
	N = 75	N = 93	% above or below the country average reported in W.A.I.T.
Germany	93%	92%	0%
Austria	95%	77%	10%
Italy	87%	73%	8%
Switzerland	89%	66%	13%
Spain	76%	63%	7%
Luxemburg	73%	61%	6%
England	61%	60%	0%
France	68%	53%	8%
Denmark	69%	44%	14%
Netherlands	61%	48%	7%
Scotland	55%	52%	2%
Portugal	63%	45%	10%
Slovenia	60%	43%	9%
Czechia	61%	41%	11%
Belgium	59%	41%	10%
Sweden	60%	40%	11%
Bulgaria	55%	39%	9%
Poland	61%	33%	15%
Finland	56%	34%	12%
Greece	59%	27%	18%
Cyprus	59%	24%	20%
Norway	45%	27%	10%
Croatia	48%	24%	13%
Ireland	35%	29%	3%
Iceland	36%	23%	7%
Estonia	29%	17%	6%
Lithuania	25%	19%	3%
Hungary	37%	8%	16%
Slovakia	28%	15%	7%
Romania	21%	13%	4%
Latvia	21%	10%	6%
Malta	13%	13%	0%
Serbia	20%	2%	10%
Bosnia and Herzegovina	11%	0%	6%
North Macedonia	12%	0%	7%
Turkey	8%	3%	3%

Source: EFPIA Patients W.A.I.T. 2025, IQVIA analysis of company size, top-20 pharma defined by 2025 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.[58] Previous analysis by the European Commission found that the number of full-time equivalents (FTEs) at agencies in Europe ranges from zero (at HIIS, Slovenia) to 604 FTEs (at NICE, England).[59]

58 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

59 Chamova, J. (2017) Mapping of HTA national organisations, programmes and processes in EU and Norway. Available at: https://health.ec.europa.eu/system/files/2018-02/2018_mapping_npc_en_0.pdf [Accessed April 2026]

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.[60] For this reason, companies are often inclined to not initiate an application until authorisation to enter the European market has been confirmed.

Transparency regarding the reason for non-filing is increasing. 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 the reasons the MAH has not filed in a particular market.[61] The fourth report documenting the results from the European Access Hurdles Portal has been published.[62]

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."[63] 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. The Commission's subsequent public report on the functioning of the Transparency Directive, published in September 2024, found that in many member states, "timelines can be challenging and that decisions are not always made within the indicated time period". There were no

60 AIFA (2024) Scientific and Economic Committee for Medicines. Available at https://www.aifa.gov.it/en/commissione-scientifica-economica [Accessed April 2026]

61 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 April 2026]

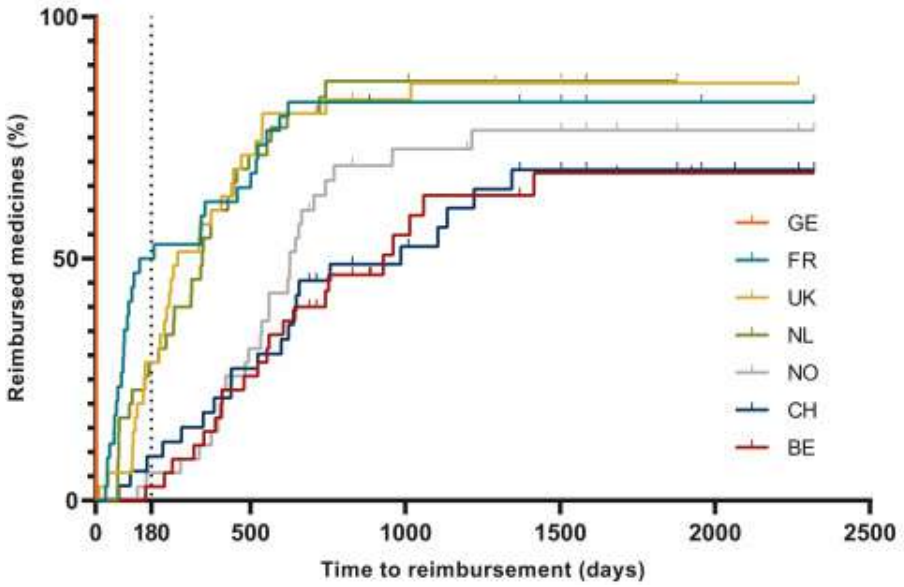
62 CRA, EFPIA (2025) European Access Hurdles Portal: Results from the third year of data collection. Available at https://www.efpia.eu/media/lrbdpuoz/cra-efpia-european-access-hurdles-portal-2025.pdf [Accessed April 2026]

63 APM Market Access (2024) No discernible progress on reviewing the EU price transparency rules. Available at https://www.apmhealtheurope.com/story/18799/87672/no-discernible-progress-on-reviewing-the-eu-price-transparency-rules [Accessed April 2024]

proposed changes to the Directive itself, but acknowledgement that its implementation needs to be strengthened.[64]

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 15). Even after taking into account delayed initiation, there are significant differences across countries. This is consistent with initial findings from the European Access Hurdles 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.[65] 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).[66]

Figure 15: Time to reimbursement of novel oncology medicines in seven high-income European countries[67]



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

There is evidence that tailored P&R approaches for different types of medicines can accelerate the P&R process. Countries with specialised P&R channels for orphan medicines, such as Finland, France, and Norway, generally have faster availability of

64 European Commission (2024) Functioning of Directive 89/105/EEC relating to the transparency of measures regulating the prices and reimbursement of medicinal products ('Transparency Directive'). Available at: https://op.europa.eu/en/publication-detail/-/publication/4f308379-762d-11ef-bbbe-01aa75ed71a1/language-en%2C [Accessed April 2026]

65 CRA, EFPIA (2025) European Access Hurdles Portal: Results from the third year of data collection. Available at https://www.efpia.eu/media/lrbdpuoz/cra-efpia-european-access-hurdles-portal-2025.pdf [Accessed April 2026]

66 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.

67 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.

orphan medicines as a result.[68,69] 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.[70] 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,[71] but it takes on average 466 days for new orphan medicines to become available to patients in Italy.[72]

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.[73] 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).

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68 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.

69 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 [Accessed April 2026]

70 Remap Consulting (2018) How is patient access to high-cost orphan drugs changing? How is patient access to high-cost orphan drugs changing? https://www.remapconsulting.com/patient-access-to-high-cost-orphan-drugs-remap-consulting/ [Accessed April 2026]

71 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.

72 IQVIA (2025) *The Patient W.A.I.T. Indicator 2024 Survey*

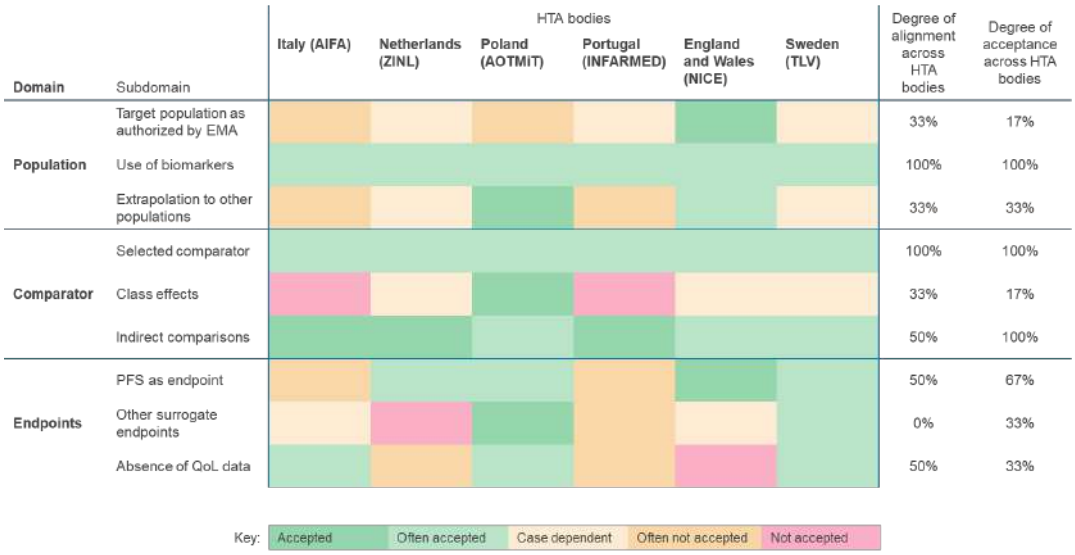
73 In the European Commission's recent evaluation of the functioning of the Transparency Directive, 17 out of 20 member states consulted referred to the existence of a clock stop procedure. Of these, 14 member states indicated that the reason for the clock stop procedure is to request more information from the MAH. Available at: https://op.europa.eu/en/publication-detail/-/publication/4f308379-762d-11ef-bbbe-01aa75ed71a1/language-en%2C [Accessed April 2026]

To illustrate the differences in evidence requirements, we can compare the evidence requirements of EMA and the HTA bodies in six case-study countries as part of the 'Time to Patient Access' project (see Figure 16). 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.

This analysis found that the overall degree of evidence acceptability by HTA bodies (of 19 different types of requirements) ranged from 37% in Portugal to 79% in Poland.[74] As illustrated in Figure 16, HTA bodies are often misaligned on the acceptability of different types of evidence, most notably demonstrated by acceptance of other surrogate endpoints (beyond progression-free survival (PFS)), where there is 0% alignment across the HTA bodies).

The level of alignment is highest for the use of biomarkers and the selected comparator, 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 PFS. As illustrated in Figure 16, 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, often not accepted in Portugal, and accepted only in a case dependent manner in England and Italy.

Figure 16: Evidentiary requirements for oncology drug assessments of six HTA bodies[75]



Source: Wolters et al. (2024)

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

74 Wolters et al. (2024) Differences in evidentiary requirements for oncology drug effectiveness assessments among six European health technology assessment bodies — can alignment be improved? *Expert Review of Pharmacoeconomics & Outcomes Research*. 24(2).

75 Wolters et al. (2024) Differences in evidentiary requirements for oncology drug effectiveness assessments among six European health technology assessment bodies — can alignment be improved? *Expert Review of Pharmacoeconomics & Outcomes Research*. 24(2).

endpoints.[76] 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. There are also an increasing number of medicines in early-stage cancers where the evidence is based on clinical trials that rely solely on surrogate endpoints.[77]

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.[78]

Looking forwards, the phased 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.[79]

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 17), 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

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

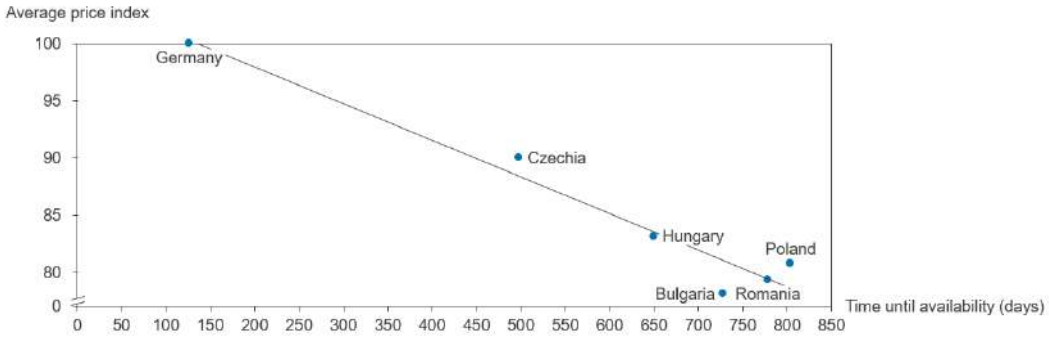
77 Thorlund, K. et al. (2024) Adapting Health Technology Assessment agency standards for surrogate outcomes in early stage cancer trials: what needs to happen? Expert Review of Pharmacoeconomics & Outcomes Research. 24(3).

78 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.

79 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 [Accessed April 2026]

usage. Other studies have failed to find a relationship between delays and prices, suggesting that expected prices do not affect the speed of launch.[80]

Figure 17: 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[81]

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.[82]

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. 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 18). 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.[83]

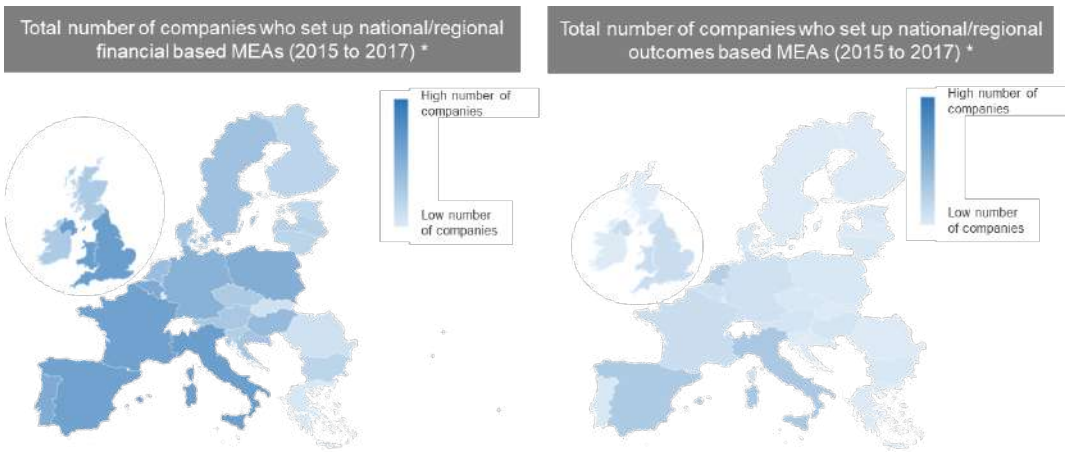
80 Time to Entry for New Cancer Medicines: From European Union–Wide Marketing Authorization to Patient Access in Belgium, Estonia, Scotland, and Sweden. Ferrario, A. Health Policy Analysis. *Value in Health* 21(7): 809–821, 01 July 2018

81 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 2026]

82 EFPIA (2023) A value-based approach to pricing. Accessible at: https://www.efpia.eu/media/677284/a-value-based-approach-to-pricing-2.pdf [Accessed April 2026]

83 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 [Accessed April 2026]

Figure 18: 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 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.[84] This may explain the decline in rates of availability observed in the Nordics over recent years.[85]

84 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 [Accessed April 2026]

85 EFPIA W.A.I.T Indicator Survey (2024)

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 19, which presents the percentage of HIV antivirals (J5C9) and PD-1s 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, however no countries have full availability to PD-1s.

Figure 19: Number of products available in a therapeutic class (the example of HIV antivirals and PD-L1s)

Source: EFPIA Patients W.A.I.T. (2025), IQVIA ATC4 class (J5C8 and J5C9 HIV Antivirals , n=8; L1G5 Monoclonal antibodies PD-1/PD-L1, n=10)

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

Insufficient budget to implement decisions

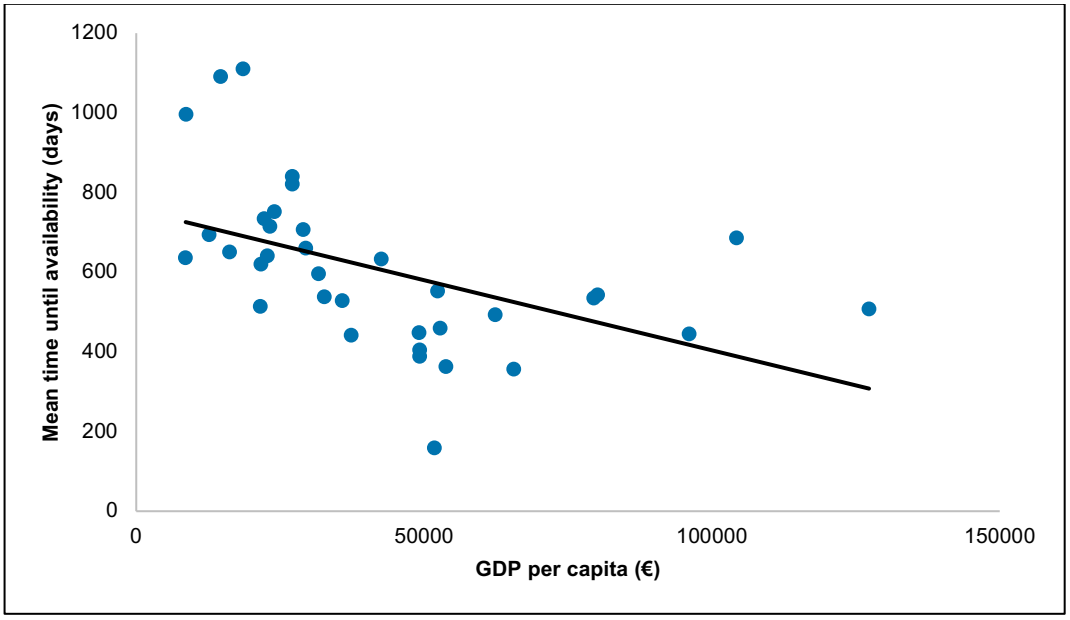
Within the EU, we clearly have countries with very different levels of income, with GDP per capita varying from €11,710 (Bulgaria) to €100,380 (Luxembourg) per annum.[86] They also have made different decisions regarding the amount they invest in health care. The data from the OECD clearly show the European differences in economic context:

86 Eurostat (n.d.). Real GDP per capita. Available at: https://ec.europa.eu/eurostat/databrowser/view/sdg_08_10/default/table?lang=en [Accessed April 2026]

- Relative healthcare spending as a percentage of overall GDP is twice as high in Germany and France (11.7% and 11.5% respectively) as in Romania and Luxembourg (5.7%).[87]
- Relative pharmaceutical expenditures as a percentage of overall GDP are more than four times higher in Greece (2.4%) than in Denmark and Luxembourg (0.6%).[88]
- Absolute healthcare spending ranges from approximately €972 per capita in Romania to €6,888 per capita in Luxembourg.[89]

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.

Figure 20: Relationship between time to availability (delays) and GDP per capita



Source: The Patient W.A.I.T. Indicator 2025 Survey, World Bank 2024

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.

87 Eurostat. (n.d.). Healthcare expenditure statistics - overview. Available at: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Healthcare_expenditure_statistics_-_overview#Healthcare_expenditure [Accessed April 2026]

88 OECD. (n.d.). Pharmaceutical Spending. Available at: https://data.oecd.org/healthres/pharmaceutical-spending.htm [Accessed April 2026]

89 Eurostat. (n.d.). Healthcare expenditure statistics - overview. Available at: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Healthcare_expenditure_statistics_-_overview#Healthcare_expenditure [Accessed April 2026]

observed a significant and robust market size effect: the launch time of new pharmaceutical products decreases as market size increases.[90]

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). The impact of health system resource constraints in smaller European markets is explored in greater detail in a new dedicated report.[91]

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 187 beds per 100,000 inhabitants in Sweden to approximately 864 in Bulgaria).[92] The infrastructure disparity is particularly evident with respect to highly specialised or orphan medicines:

- 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.[93] 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. Country-level studies have identified the absence of public funding for testing as the main barrier to uptake.[94] 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 (Figure 21).[95] In more than half of OECD countries reimbursement of companion diagnostics is not coupled with the reimbursement of medicines, leading to a situation where only the

90 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

91 CRA Root causes of unavailability and delay in smaller markets report, May 2025

92 Eurostat (2025) Healthcare resource statistics - beds, 2025. Available at: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Healthcare_resource_statistics_-_beds [Accessed April 2026]

93 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.

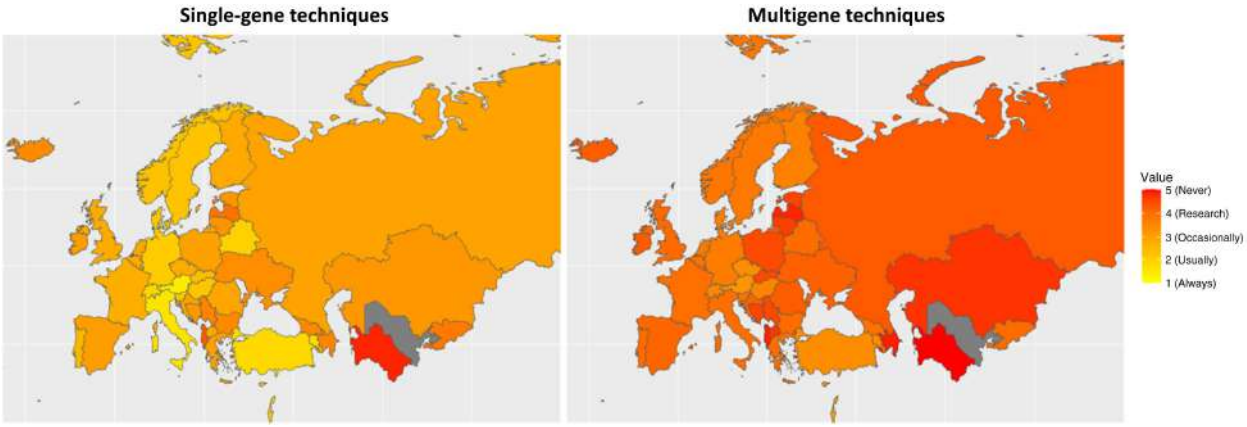
94 Mestre-Ferrándiz, J., et al. (2024). Expert-based collaborative analysis of the situation and prospects of biomarker test implementation in oncology in Spain. Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico, 26(4), 985–990. https://doi.org/10.1007/s12094-023-03338-8

95 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.

medicine is made available without the companion diagnostic.[96] 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.[97]
- 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.

Figure 21: Access to precision oncology biomarker testing in Europe



Source: Bayle et al. (2023)[98]

In many countries, the availability of scientifically robust epidemiological data for individual rare diseases varies greatly; such data may not be available at all.[99] 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

96 Hofmarcher T., Berchet C., Dedet G. OECD Publishing; Paris, France: 2024. Access to Oncology Medicines in EU and OECD Countries Available at https://www.oecd.org/en/publications/access-to-oncology-medicines-in-eu-and-oecd-countries_c263c014-en.html [Accessed April 2026]

97 Hofmarcher, T., Charalambous, A., Normanno, N., Szmytke, E., & Wilking, N. (2025). Access to novel cancer medicines in Europe: inequities across countries and their drivers. ESMO open, 10(10), 105810. https://doi.org/10.1016/j.esmoop.2025.105810

98 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.

99 Ferreira, C. R. (2019) The burden of rare diseases. *AJMG*. 179(6), p885–892.

systems, which need to map out their specialised healthcare services and budget impact.[100]

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,[101] which can also provide a means for evidence generation to support payer decision-making.[102] 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.[103]

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, 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.[104] There have

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

101 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

102 Polak, T. B. et al. (2022) Generating Evidence from Expanded Access Use of Rare Disease Medicines: Challenges and Recommendations. *Front. Pharmacol.* 13.

103 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 2026]

104 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 2026]

also been studies looking at different types of medicine: time to regional access to orphan medicines following the national decision is 224 days on average.[105]

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 Access[106] 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:

- 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.[107] Yet in both the inpatient and outpatient sectors, a medicine must be included on the reimbursement list before it is used.[108]
    - In Bulgaria, the reimbursement list is updated on a predictable schedule: once a year in January.[109] 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.

Table 3: Frequency of publication of P&R decisions across select European countries

Country	Frequency of updates to positive reimbursement list
Bulgaria	Once per year

105 Marino, M. L. et al. (2023) Orphan drugs in Italy: availability and time-to-access at regional level. *GRHTA*. 10(1).

106 Vintura (2020, July) Every Day Counts. Available at: https://www.efpia.eu/media/578013/every-day-counts.pdf [Accessed April 2026]

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

108 WHO (2018) Medicines reimbursement policies in Europe. Available at: https://www.who.int/europe/publications/i/item/9789289053365 [Accessed April 2026]

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

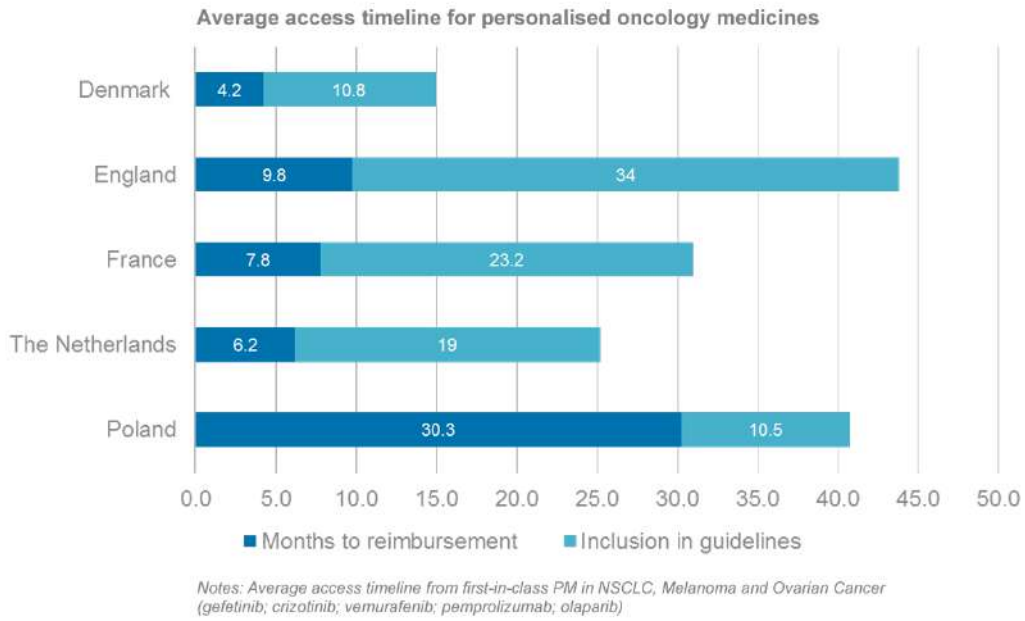
Croatia	Ad hoc
Czechia	Monthly
Estonia	Four times per year
Greece	Twice per year
Hungary	Ad hoc
Latvia	Ad hoc
Lithuania	Ad hoc
Montenegro	Three times per year
North Macedonia	Ad hoc
Poland	Every two months
Romania	Twice per year
Slovakia	Four times per year
Slovenia	Monthly

Source: CRA analysis of national HTA websites and interviews with national pharmaceutical trade associations

- Clinical guidelines do not always include the most recent therapeutic innovations, even in larger Western European countries. For example, in France, updates to the French National Authority for Health's 2013 guidelines for diabetes were delayed by nine years; despite the reimbursement of many new medicines and drug classes over this period, the new guidelines were only published in 2024.[110] 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 22).

110 Haute Autorité de Santé (2013) "Stratégie thérapeutique du patient vivant avec un diabète de type 2". Available at: https://www.has-sante.fr/jcms/p_3191108/fr/strategie-therapeutique-du-patient-vivant-avec-un-diabete-de-type-2 [Accessed April 2026]

Figure 22: Average access timeline for personalised oncology medicines

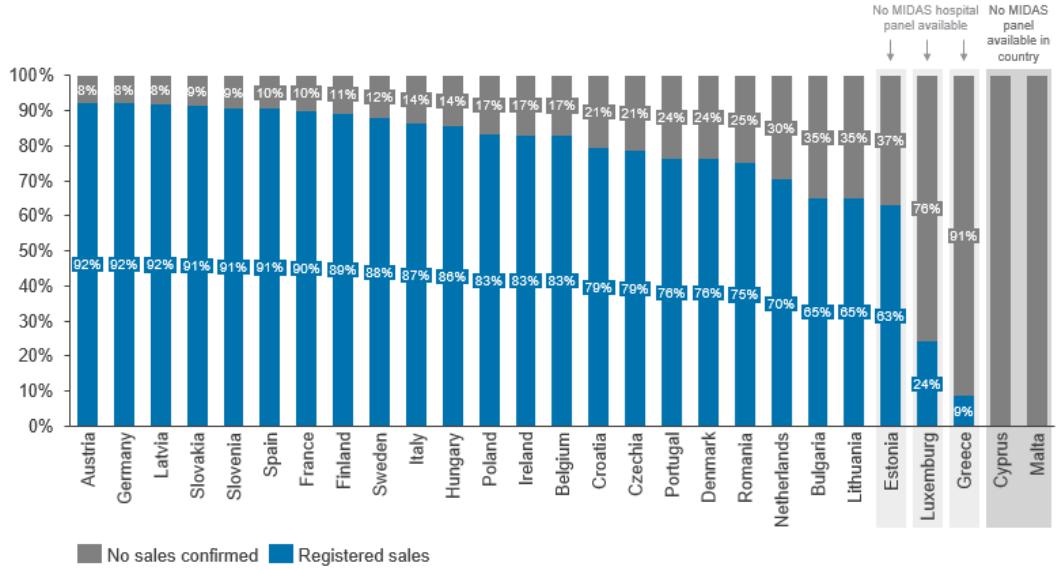


Source: EBE Personalised Medicine Report (2018)[111]

- 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 79% of products available in the Czech Republic (see Figure 23). Unsurprisingly, not all companies choose to apply for reimbursement in these markets.

111 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 2026]

Figure 23: Percentage of available products with no recorded sales in each EU country

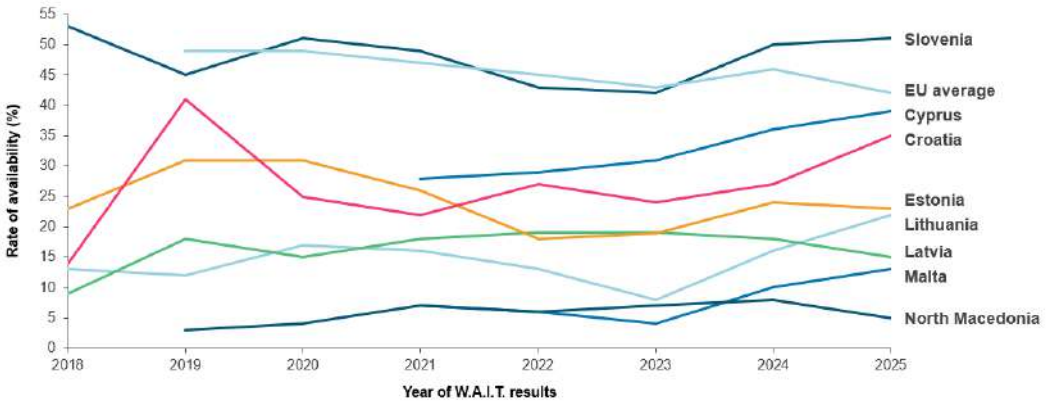


Source: The analysis includes available products in each country and evaluates whether they have recorded sales (IQVIA MIDAS sales data 2015-2025). In each country, "Sales" is defined as available in WAIT indicator and showing sales in IQVIA MIDAS. "No sales" is defined as available in WAIT indicator and showing no sales in IQVIA MIDAS since 2015. Sales data reflects sales recorded within each country. 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. A focus on root causes for unavailability and delay in smaller European markets

An area of increased scrutiny has been whether the root causes are similar in smaller European markets. This has focused on markets such as Croatia, Cyprus, Estonia, Latvia, Lithuania, Malta, and Slovenia; and two non-EU countries (included to examine the impact of local regulatory processes in smaller markets): Montenegro and North Macedonia. Overall, the level of availability is significantly lower that the European average and this has been consistent since 2019. This picture has not changed with the new W.A.I.T. data.

Figure 24: Rates of availability of innovative medicines in smaller markets[112]



Source: The Patient W.A.I.T. Indicator Surveys[113]

Although many of the root causes are common across all markets, there are specific issues in three areas: the pricing and reimbursement process; the value assessment process; health system constraints and resources.

In terms of:

- Price and reimbursement process: there are specific issues associates to capacity constraints, lack of transparency or ability to monitor the outcomes of decision-making processes, and lack of adherence to regulations on P&R timelines.
- Value assessment process: the size of these markets inevitably leads to small patient populations and lack of availability of local epidemiological data. Another evidence challenge can be described as both a symptom and a cause of unavailability of innovative medicines in smaller markets: because these markets generally are slower to adopt innovative medicines (as shown in W.A.I.T.), the local standard of care in the country may not align with the international standard of care.
- Health system constraints and resources: many of the smaller markets in scope of this study spend less on healthcare and on pharmaceuticals per capita than the EU average. Smaller markets, with smaller healthcare budgets, are also taking different decisions regarding the proportional allocation of the healthcare budget to pharmaceuticals. The extent of the challenge in smaller markets is particularly evident for orphan medicines and precision oncology treatments that often require diagnostic testing infrastructure and a network of experts to diagnose and treat patients.

112 Note: Montenegro is not including in the W.A.I.T. Indicator Survey. Malta and Cyprus were included for the first time in 2022. North Macedonia results should be interpreted with the context that rates of availability are in reported by W.A.I.T. in context of EMA approvals, but North Macedonia makes its own marketing authorisation decisions which may differ to those of the EMA. More generally, the geographic scope, methodology and reporting on the W.A.I.T. Indicators has evolved over time and hence caution should be applied when making year on year comparisons.

113 IQVIA (various) EFPIA Patients W.A.I.T. Indicator 2018-2023 Surveys. Latest available at: https://efpia.eu/media/vtapbere/efpia-patient-wait-indicator-2024.pdf [Accessed April 2026]

1.8. 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 to[114]

- 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.[115]

1.9. The impact of the global policy environment and geopolitical tensions

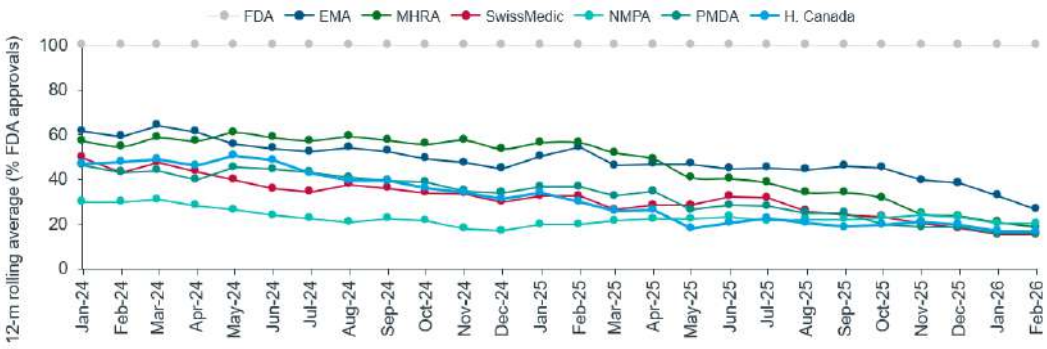
As set out above it is too early for the W.A.I.T. data to capture any impact from the changing global policy environment, particularly if MFN has had any impact on availability. The impact of these changes could be significant going forward however, so it is will be important to look for early indicators and track these over time. New regulatory approval indicators have been developed that monitor the extent to which FDA approvals are followed by approvals in other regions. In recent years, the number of EMA approvals as a percentage of FDA approvals has been declining in Europe. If we look at the last year, including the announcement of introduction of MFN we can see if this trend changes. Given this analysis is based on regulatory approvals, rather than submissions, we need to be cautious of any impact at this stage. Although not statistically significant, there is an apparent acceleration in the trend from October 2025. (Figure 25).[116] While it is too early to determine the full effect of this policy, the trend is concerning and should be monitored closely.

114 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/

115 Vintura (2021, November) 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 April 2026]

116 IQVIA (2026) Regulatory approval assessments in the EU and comparator countries (QTR). 10th April 2026

Figure 25: Approvals by leading regulators of FDA approved medicines - 12-month rolling average (% FDA approvals)[117]



Source: IQVIA analysis of EMA, FDA, MHRA, Health Canada, NMPA, PMDA, SwissMedic (2026)

1.10. 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 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,[118] and recognise that 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 Novel Medicines Platform undertaken 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.[119] 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. To achieve this goal, the industry also proposes the establishment of structured dialogue (s) to find practical solutions if products are not available four years after marketing authorisation approval.

However, no single commitment, or indeed regulatory requirement, can address unavailability and delay, and a package of policy proposals is needed.

117 Medicines are considered a NAS if at least one active ingredient has not been previously marketed globally. For 2026 approvals include NAS approved in any country considered in the analysis between Jan1st and 28th Feb 2026. Medicines approved in at least one of the seven countries were included within the scope of the analysis. For instance, FDA approvals include NAS that have not been approved by the EMA, Health Canada, PMDA, NMPA, MHRA, or Swissmedic.

118 Reform of EU pharmaceutical legislation (2025, December) Available at: https://health.ec.europa.eu/medicinal-products/reform-eu-pharmaceutical-legislation_en [Accessed April 2026]

119 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 2026]

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.[120] 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 will provide an opportunity to reinforce expertise-driven assessment and enable a more agile, centralised authorisation framework. The European Commission's revisions 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.[121] Further, a number of provisions in the revised rules 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 will 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.

The proposed Biotech Act could also improve the clinical trial environment, if appropriately designed and implemented. In particular, the ambition to reduce clinical trial approval timelines to 75 days would make Europe considerably more attractive for innovative or time-critical trials. In addition, the coordinated assessment for combined studies and EMA support for competent authorities in the context of multi-country clinical studies, the new criteria for breakthrough and orphan devices, the creation of a dispute resolution mechanism, increased flexibility for in-house devices and an enhanced role of expert panels should make undertaking clinical trials in Europe easier. Accelerating the regulatory approval timeline is even more important given the potential impact from MFN.

120 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.

121 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.

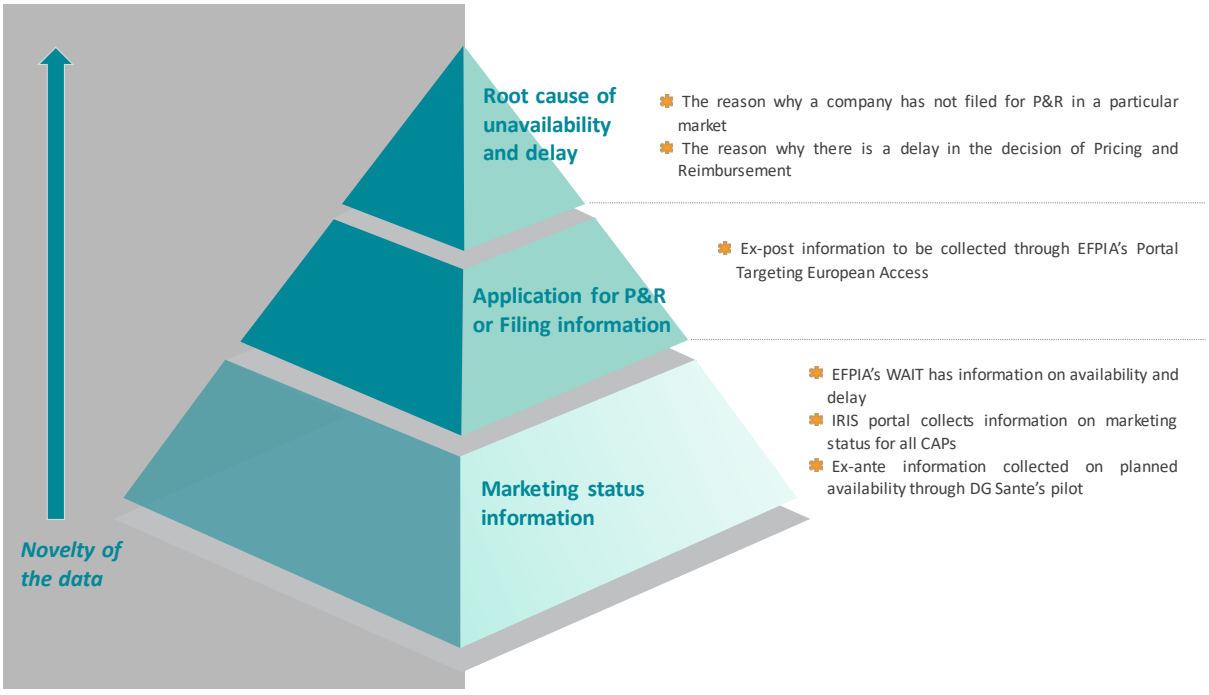
Proposals that aim to increase transparency of information regarding placing centrally approved products on the market (Figure 26)

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 (Figure 27).

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.

Figure 26: 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.[122] These analyses have shown for the first time the percentage of products that have been filed for P&R or reimbursed following marketing authorisation and showed that, even including products that have only recently been approved, the majority have

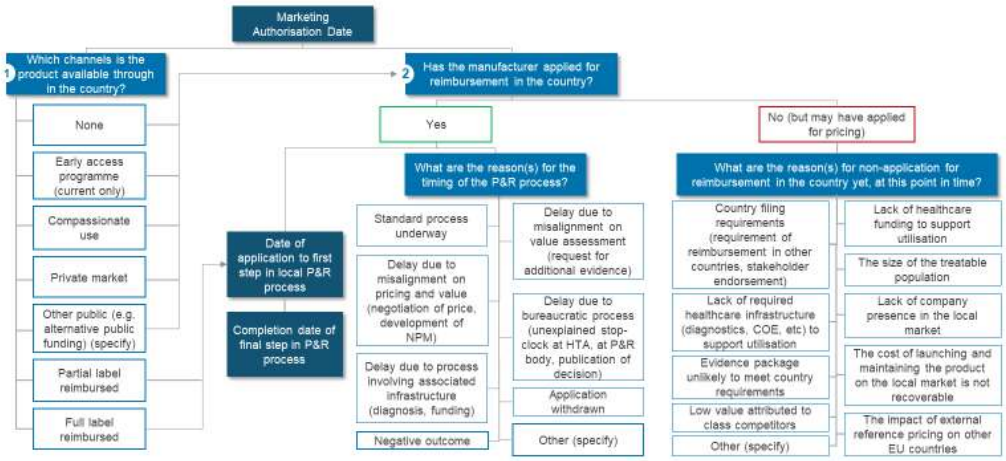
122 CRA, EFPIA (2023) European Access Hurdles Portal: initial results. Available at: https://www.efpia.eu/media/677291/european-access-hurdles-portal-efpia-cra-report-200423-final.pdf [Accessed April 2026]

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 fourth review of results from the portal is being published separately in April 2026 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 fifth year of operation, 100% of EFPIA members with products eligible for inclusion in the portal submitted data, providing information on 91 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.

Figure 27: Data captured by the portal



The role of the Portal in assessing the factors affecting unavailability and delay will be particularly important in tracking the impact of MFN and policies introduced to mitigate its impact. The introduction of new regulatory indicators tracking whether products approved in the US are subsequently approved in Europe, will provide the earliest evidence of this.

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.[123,124]

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.
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. This is also an important mechanism that can be used, instead of arbitrary clawbacks to help provide budget certainty. They can also be used in association with an increase in European health spending, to ensure spending is focused on areas delivering value to patients and the healthcare system. However, they need to negotiated in a fashion that ensures compliance with Transparency Directive.

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—are predominantly the same for all markets. This occurs because HTA agencies adopt different approaches to

123 EFPIA (2020, July) Addressing Healthcare Challenges. Novel Pricing and Payment Models: New solutions to improve patient access. Available at https://efpia.eu/media/554543/novel-pricing-and-payment-models-new-solutions-to-improve-patient-access-300630.pdf [Accessed April 2026]

124 EFPIA (2021, April) Addressing Healthcare Challenges. Principles on the Transparency of Evidence from Novel Pricing and Payment Models. Available at https://www.efpia.eu/media/602581/principles-on-the-transparency-of-evidencefrom-novel-pricing-and-payment-models.pdf [Accessed April 2026]

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 now applies to oncology and ATMP products, and will be extended to orphan medicinal products in three years 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 minimise delays to the overall access timelines. Ensuring that EU HTA accelerates access to medicines in Europe and does not introduce an additional barrier is even more important given the context of the MFN.

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) and for ensuring availability to innovation as soon as possible**. 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 preventing launch on day 1 and the application of differential pricing must also be addressed, including the use of external reference pricing and extraterritoriality. EFPIA members support an EBTP approach based on a concrete conceptual framework[125] 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 EBTP concept can be extended to work within a wider framework allowing flexibility to set prices in the private market, allow freedom for companies to set the public list price (within a national framework for pricing and reimbursement) and ensuring access immediately after marketing authorisation. This is a mechanism that could be used to increase European health spending in a way that is consistent with value-based pricing, equity and improved availability of medicines in Europe. 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.

1.11. 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, accompanied with underlying evidence. In this regard, the industry considers that clarity and predictability for both Marketing Authorisation Holders and Member States will be critical to ensuring that the market and supply provisions related to centrally authorised products in the revised EU pharmaceutical legislation are implemented effectively, to the benefit of improved access for all EU citizens.

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 to patients.
- **Market launch:** This refers to a product being placed on the market for sale (not to its reimbursement by the national or regional authorities).