

The root cause of unavailability and delay to innovative medicines: Reducing the time before patients have access to innovative medicines

Executive Summary¹

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

EFPIA for many years has looked at the length of time it takes for medicines to be made available. As illustrated by the most recent data in the Patient W.A.I.T. Indicator Survey in 2021, the average time to reimbursement for innovative treatments across EU and European Economic Area (EEA) countries continues to be as long as 511 days, ranging from 133 days in Germany to over 899 days in Romania. There are patient access inequities within Europe, with significant differences across countries in the number of products that are available at a point in time and that the time taken prior to national reimbursement also varies significantly from one country to another. The industry shares concerns about these delays and recognises that delays and the unavailability of medicines harm patients. Moreover, there is need to address delays as European economies and healthcare systems recover from COVID-19.

Over the past two years, EFPIA has documented the root cause of access inequality and found there are 10 interrelated factors that explain unavailability and delay (defined as length of time from European marketing authorisation to availability at Member State level) to innovative medicines, building on the WAIT analysis.⁴ These are rooted in the medicines access systems and processes in the EU member states and the corresponding impact on commercial decision-making. They range from a slow regulatory process to late initiation of market access assessment, to duplicative evidence requirements, to reimbursement delays, and local formulary decisions. As the root causes are multifactorial, they can only be solved by different stakeholders working together.

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

² See EFPIA Pipeline Review 2021 Update, IQVIA project report, February 2021. Accessible at: https://www.efpia.eu/media/602564/iqvia_efpia_pipeline-review_final.pdf

³ This paper focuses primarily on root cause of delay for centrally approved products by the EMA. It should be noted that there are non-centrally approved medicines for which many of these root causes would also apply.

⁴ <https://www.efpia.eu/publications/downloads/efpia/the-root-causes-of-unavailability-and-delay-to-innovative-medicines/>

Figure 1: The root causes of delays and unavailability

Category	Potential root causes
The time prior to market authorisation	1. The speed of the regulatory process 2. Accessibility of medicines prior to marketing authorisation
The price and reimbursement process	3. Initiation of the process 4. The speed of the national timelines and adherence
The value assessment process	5. Misalignment on evidence requirement 6. Misalignment on value and price 7. The value assigned to product differentiation and choice
Health system readiness	8. Insufficient budget to implement decisions 9. Diagnosis, supporting infrastructure and relevance to patients
Delay from national to regional approval	10. Multiple layers of decision-making processes

The industry considers that the root causes of unavailability and delay could be addressed through collaborative work with Member States, European Commission and other stakeholders on proposals to improve availability and reduce delays. These must start from the beginning of the process, including proposals to speed up the regulatory process, delivering safe and high-quality diagnostics, vaccines and treatments to patients as fast as possible. The industry welcomes the commitment to address regulatory barriers. However, these will not improve patient access to innovative medicines by themselves. EFPIA and its members have worked on a series of concrete access proposals to improve patient access to innovative medicines and reduce inequalities across Europe. These include inter alia:

- **A commitment from the industry to file pricing and reimbursement applications in all EU countries no later than 2 years after EU market authorisation.** 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.
- **The creation of a portal where marketing authorisation holders (MAH) can provide timely information regarding the timing and processing of pricing and reimbursement (P&R) applications in the various EU-27 countries,** including the reasons why there is a delay in the P&R decision or why the MAH has not filed in a particular market.
- **A conceptual framework for Equity-Based Tiered Pricing (EBTP),** to ensure that ability to pay across countries is considered in the prices of innovative medicines, anchored in a principle of solidarity between countries, to reduce unavailability of new medicines and access delays.
- **Novel payment and pricing models,** 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, whilst providing sufficient incentives for innovation.^{5,6}

- Contributing to achieving an **efficient system of European assessments of relative efficacy at time of launch** in the context of the implementation of the HTA Regulation.

The present report is the third edition of the root cause analysis first released in June 2020, which was used as a basis for discussion with several EU and national policy-makers 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 five years and the promise of the industry pipeline provides an important opportunity to improve outcomes for patients. Innovative medicines have already significantly increased survival, delivering treatments to patients with chronic diseases and those with previously untreatable cancers, treating genetic conditions for which there were no existing medicines and eliminating some infectious diseases.

There is common agreement that the value of innovation is only realised 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.⁷

The importance of the addressing unavailability and delays was highlighted in EU Pharmaceutical Strategy (see Box 1).

⁵ <https://efpia.eu/media/554543/novel-pricing-and-payment-models-new-solutions-to-improve-patient-access-300630.pdf>

⁶ <https://www.efpia.eu/media/602581/principles-on-the-transparency-of-evidence-from-novel-pricing-and-payment-models.pdf>

⁷ <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/>

Box 1: Discussion of root causes in the EU Pharmaceutical Strategy

“Innovative and promising therapies do not always reach the patient, so patients in the EU still have different levels of access to medicines. Companies are not obliged to market a medicine in all EU countries; they may decide not to market their medicines in, or withdraw them from, one or more countries. This can be due to various factors, such as national pricing and reimbursement policies, size of the population, the organisation of health systems and national administrative procedures resulting in smaller and less wealthy markets in particular facing these problems.”

Source: European Commission, EU Pharmaceutical Strategy⁸

The European Commission is currently preparing a revision of the EU Pharmaceutical Legislation and has put forward a range of proposals to address patient access inequalities across EU member states. This includes stepping up co-operation with and among Member States on the affordability of medicines. We understand that some of the proposals being discussed could introduce obligations for Marketing Authorisation Holders (MAHs) to market or supply all EU Member States. The industry has concerns regarding the use of regulatory tools designed for medicines authorisation being applied to address availability issues that are within the remit of Member States. In most countries, the inclusion of the product on the reimbursement list will determine availability and access. Any requirement for MAHs to place a centrally authorised medicine on the market in the majority of Member States (including small markets) within a certain period from authorisation, or any provision allowing early entry of generics in the EU market if a centrally authorised medicine is not launched in all Member States within a given number of years of granting the marketing authorisation, could have the opposite effect on developing and commercialising innovation on several Member States' publicly funded markets, significantly reducing patient access to innovation.

The industry shares the concern about these delays, recognises that delays and the unavailability of medicines harm patients, and agrees that there is a need to act urgently to address these longstanding issues. The purpose of this paper is to explain the different factors that could explain unavailability and delay for patients across the EU and the degree to which these are supported by the 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 have to be reached before patients have access to it (see Figure 1):

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

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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

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

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

Figure 1: After ten years of research and development, three milestones must be reached to bring innovative therapies to patients (EFPIA, 2020)

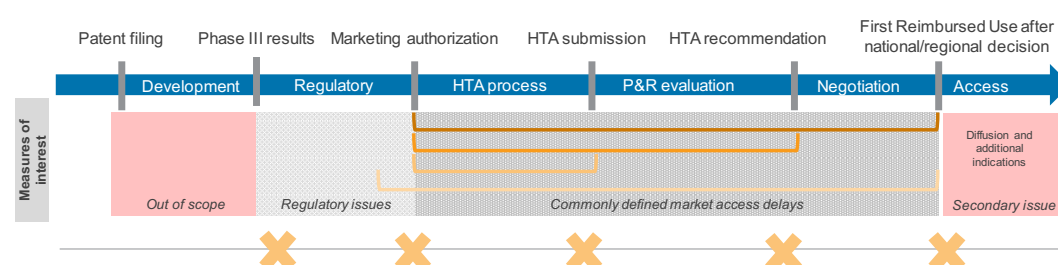


Source: EFPIA 2020

It is important to distinguish between a number of different time points:

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

Figure 2: Different types of delay

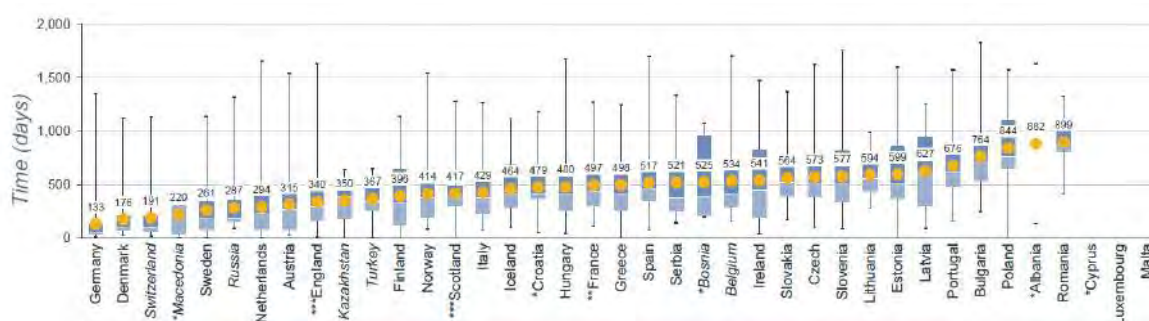


Source: EFPIA 2020

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 survey in 2020 (in Figure 3 below), the average time to reimbursement for innovative treatments across EU and European Economic Area (EEA) countries continues to be as long as 511 days, ranging from 133 days in Germany to over 899 days in Romania.

Figure 3: Median time to availability in days (2017–2020) ⁹



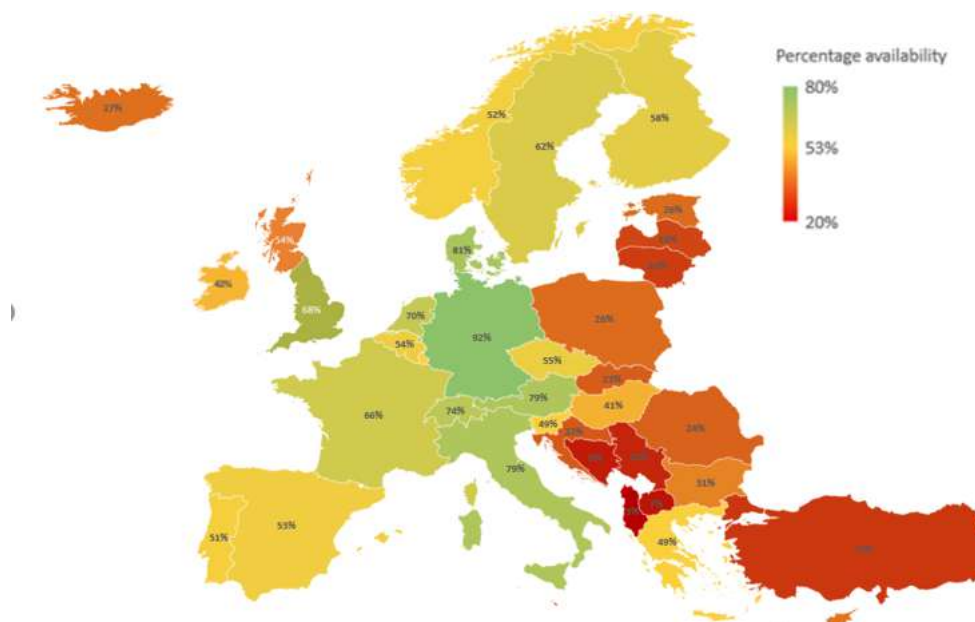
Source: *The Patients W.A.I.T. Indicator 2021*

Patients in different countries can wait more than seven times longer than patients in other countries to get access to the same medicine.¹⁰ There are some common patterns: typically, patients in Northern and Western Europe get access to new treatments between 100 and 200 days after market authorisation has been granted, whereas patients mainly in Southern and Eastern Europe wait between 600 and 1000 days. This means that at any point in time, availability of medicines varies dramatically across Europe.

⁹ European Union average: 511 days (mean %) In most countries availability equates to granting of access to the reimbursement list, except in DK, FI, NO, SE some hospital products are not covered by the general reimbursement scheme. *Countries with asterisks did not complete a full dataset and therefore availability may be unrepresentative **In France, some innovative products without competitors can be made available prior to market authorisation under the system of Temporary Authorisations. As these are not taken into account in the analysis, the average for France would be lower. ***In the UK, MHRA's Early Access to Medicines Scheme provides access prior to marketing authorisation but is not included within this analysis, and would reduce the overall days for a small subset of medicines.

¹⁰ <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/>

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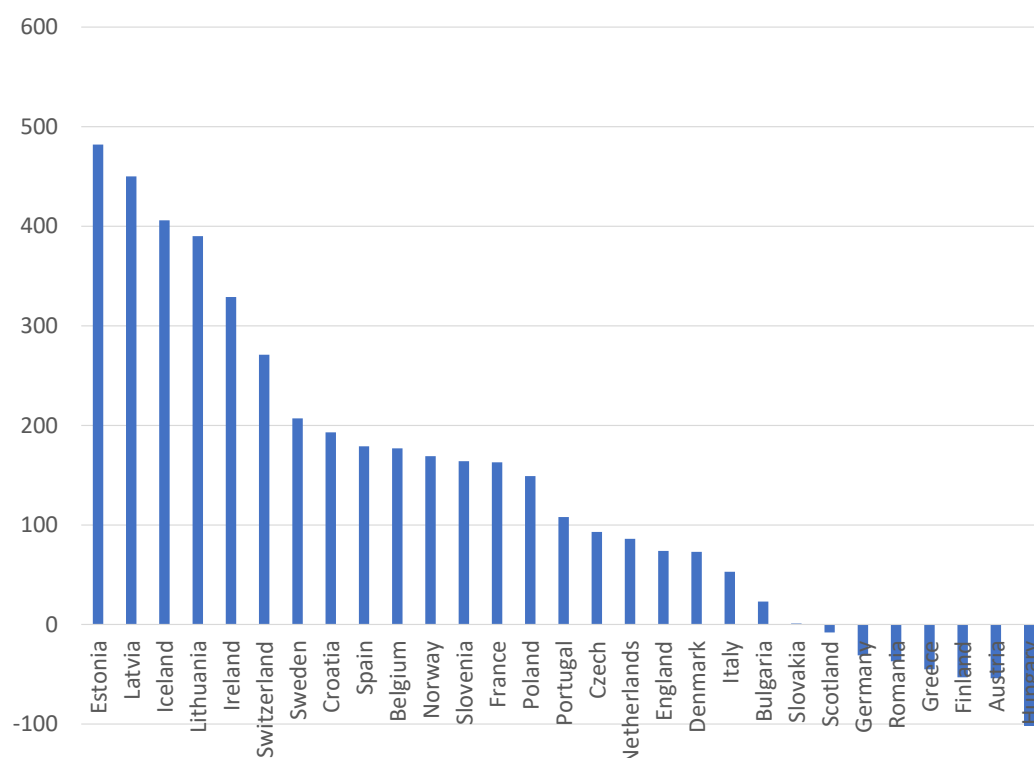
Figure 4: Comparing access across European countries

Source: *The Patients W.A.I.T. Indicator 2021*

There is also evidence that shows systematic differences between different types of medicines that has been examined in the updated W.A.I.T. analysis. Although access to oncology medicines appears to be improving, access to orphan medicines continues to vary considerably across EU member states, with long delays and low availability in Central and Eastern Europe.

Figure 5: Difference in the median time to availability for all medicines vs orphan medicines (2017 – 2020) – positive means orphan are slower than all medicines by number of days

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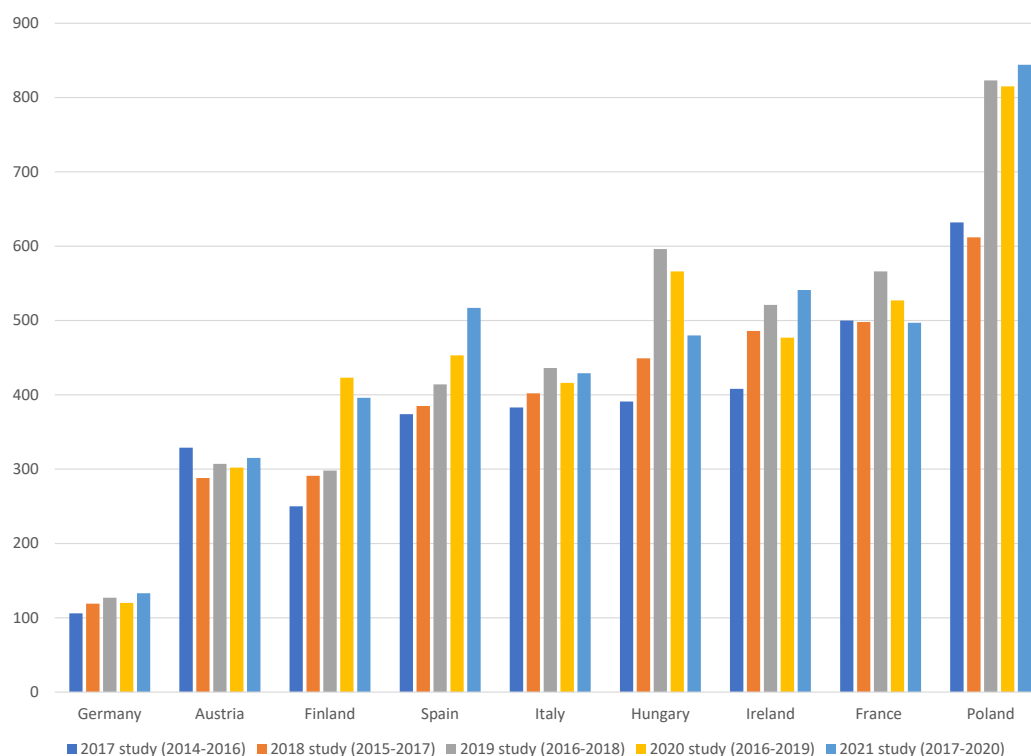
Source: *The Patients W.A.I.T. Indicator 2021*

Even within one country, patients can get access to some medicines almost immediately and wait years for others. For example, in Finland the shortest delay was 0 days and the longest 1676 days, in France the variance was 112 days to 1772 days, and in Spain 41 days to 1676 days.

It is important to consider whether delays are getting longer or shorter over time. If we look across all innovative medicines, there is little evidence that delays are reducing – in fact the contrary.¹¹ This is likely to become an even bigger concern as we consider the consequences of COVID-19.

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This will vary by therapeutic area. According to academic analysis, median times from marketing authorisation to first use of cancer medicines were shorter for medicines launched between 2010 and 2014 versus sample-wide (2000–2014). 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

Figure 6: Comparison of delay over time (median delays in days)

Source: *The Patients W.A.I.T. Indicator 2021*

The analysis set out is broadly consistent with the recent Organisation for Economic Co-operation and Development (OECD) analysis of the availability of oncology medicines. This found significant differences in availability, with the largest percentage of product/indications approved in Denmark and Germany (91% and 88% respectively). Malta had the lowest percentage of pairs approved and covered 46%.

1.4. What are the factors that could explain unavailability and delay?

The cause of delays and unavailability has been the subject of debate for many years. Policymakers and non-governmental 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 often delays access to medicines. In reality, there are many interconnected factors that 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 on the market (see Section 1.6). Given this, it is unsurprising that other manufacturers might choose to avoid the cost of applying for reimbursement.

- In other markets, it is a requirement that a product is already reimbursed in a series of other comparable countries.¹² Again, it should be no surprise that application for reimbursement is delayed until access on these markets is achieved.

In other words, the environment affects commercial decisions. This paper seeks to untangle these factors. EFPIA has identified 10 factors from 5 different perspectives: the time prior to market authorisation; the pricing and reimbursement process; value assessment criteria; health system readiness; and delay from national to regional approval.

Figure 7: The root causes of unavailability and delay

Category	Potential root causes
The time prior to market authorisation	1. The speed of the regulatory process 2. Accessibility of medicines prior to marketing authorisation
The price and reimbursement process	3. Initiation of the process 4. The speed of the national timelines and adherence
The value assessment process	5. Misalignment on evidence requirement 6. Misalignment on value and price 7. The value assigned to product differentiation and choice
Health system readiness	8. Insufficient budget to implement decisions 9. Diagnosis, supporting infrastructure and relevance to patients
Delay from national to regional approval	10. Multiple layers of decision-making processes

Source: EFPIA

We now turn to the evidence on what causes unavailability but agree with the caution set out in the OECD analysis, that we 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.”¹³

1.5. Root causes of unavailability and delay

1.5.1. The time prior to marketing authorisation

The first set of root causes to investigate relate to delay prior to marketing authorisation. The granting of a centralised marketing authorisation by the European Medicines Agency (EMA) covering all EU countries takes away 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.

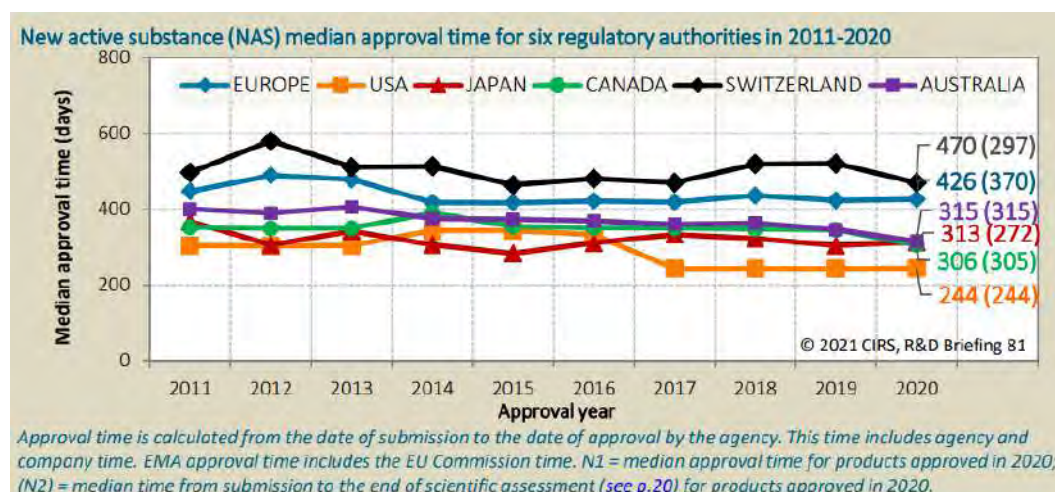
The speed of regulatory process

¹² Greece: article 22 of Law 4633/2019: medicines with patent protection are subject to health technology assessment (HTA) in Greece only if they are reimbursed in 5 other countries with HTA process from the following list: Austria, Belgium, France, Germany, Denmark, Spain, Netherlands, Italy, Portugal, Sweden and Finland.

¹³ Addressing Challenges in Access to Oncology Medicines, Analytical Report. OECD, April 2020.

Although this is not captured in EFPIA's W.A.I.T. indicator, the time from application to granting of marketing authorisation has been examined in many different papers. Looking at recent evidence on new active substances it is clear that the European regulatory process is slower than some international processes, particularly that of the US (Figure 3 below).¹⁴

Figure 8: Comparison of length of time of market authorisation process



Source: https://cirsci.org/wp-content/uploads/dlm_uploads/2021/06/CIRS-RD-Briefing-81-6-agencies-v5.pdf

Many recent studies have focused on cancer medicines:

- For 29 cancer drugs approved by the EMA between 2006 and 2011, one study looked at approval times in three major jurisdictions. Median approval time was shorter in the United States (US) (6.0 months) than in Japan and Europe (15.0 and 13.3 months, respectively).¹⁵
- Another study, focusing on 16 tyrosine kinase inhibitors (TKIs) approved by the US Food and Drug Administration (FDA) as of 30 September 2012, found the average time spent on review and approval between the US (205.3 days) and the EU (409.6 days).¹⁶ The active review time was similar in both jurisdictions, 205.3 days in the US and 225.4 days in the EU, with the differences attributed to longer clock stops during the review process to collect additional information from sponsors, and the

¹⁴ This does vary by pathways. As reported in Rodier et al. (2019), The overall median approval time taken by 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, Céline, Magdalena Bujar, Neil McAuslane, and Lawrence Liberti. 2019. *New Drug Approvals in Six Major Authorities 2009-2018: Focus on Facilitated Regulatory Pathways and Orphan Status*. London, UK.

¹⁵ Hartmann, M., Mayer-Nicolai, C. and Pfaff, O. Approval probabilities and regulatory review patterns for anticancer drugs in the European Union. *Critical Reviews in Oncology/Hematology* 87(2): 112–121

¹⁶ A fresh perspective on comparing the FDA and the CHMP/EMA: approval of antineoplastic tyrosine kinase inhibitors. Shah et al. *British Journal of Clinical Pharmacology* 76(3): 396–411

time from recommendation by the advisory opinion, and the decision of the European Commission.

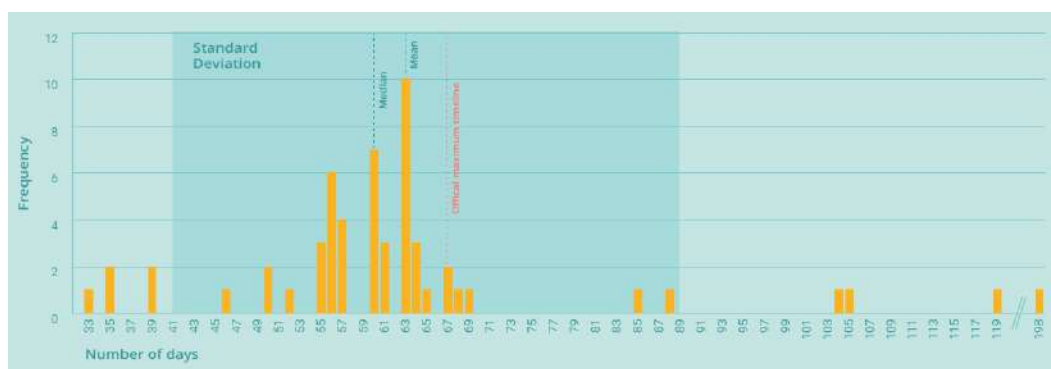
- For 37 cancer medicines approved between 2005 and 2013 by Health Canada, the time from date of submission to approval was much longer for the EMA and Health Canada than for the FDA, by an average of 6.7 months and 6.4 months, respectively.¹⁷ Submissions to the FDA were also made on average 12.9 and 28.4 months earlier than submissions to Health Canada and to the EMA, respectively.
- A recent study reported median approval times for oncology drugs and immunomodulators between 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 (JPMDA) (284 days) and the FDA (239 days).¹⁸
- The study results show that in the time period between 2011 and 2015 the FDA approved 170 new drugs while the EMA approved only 144. Furthermore, the FDA had a median review time of 306 days, while at the EMA there was a median review time of 383 days. Encouragingly for rare disease patients in the US, there were considerably more orphan drug approvals at the FDA than there were at the EMA. 43.5% of the approved agents in the US were orphan drugs, while in Europe only 25% were orphan drugs.¹⁹
- The OECD recently repeated this analysis for oncology reports, finding that the average delay was 13 months for the EEA, 7 months for the US.²⁰

For other categories of medicine, the difference may be smaller but the FDA is still faster than the EMA.²¹

For Europe this includes a period between the CHMP opinion and the EC decision.

Figure 9: Overview of timelines between CHMP opinion and EC decision, for all oncology therapies evaluated by the CHMP between 2016 and 2020 (new molecular entities only).

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- 17 Cross-comparison of cancer drug approvals at three international regulatory agencies. Samuel, N. and Verma, S. *Current Oncology* 23(5): 454–460
- 18 The Centre for Innovation in Regulatory Science (CIRS), 2020
- 19 Regulatory Review of New Therapeutic Agents — FDA versus EMA, 2011–2015 <https://www.nejm.org/doi/full/10.1056/NEJMc1700103#t=article>
- 20 Addressing Challenges in Access to Oncology Medicines, Analytical Report. OECD, April 2020.
- 21 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 Minette-Joëlle Zeukeng, Enrique Seoane-Vazquez and Pascal Bonnabry. 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), (2018).



Source: *Every Day Counts, Improving regulatory timelines to optimise patient access to innovative oncology therapies in Europe*, Vintura, November 2021

Some argue that this reflects that Europe is losing ground in terms of priority of regulatory approval and this will only get worse in the future.²² However, even today there is often a significant delay caused by the marketing authorisation process.

Accessibility of medicines prior to marketing authorisation

In reality, it is possible for patients to access medicines prior to marketing authorisation in some countries.^{23, 24} Funded early access schemes represent temporary reimbursement pathways that ensure direct patient access to new promising treatments prior to regulatory approval, where there is a clear unmet need.²⁵

Some countries have introduced early access schemes specifically aimed at providing immediate patient access for products prior to a full marketing authorisation (MA) being granted. Some countries, such as France and England, have introduced a more systematic approach. For example in France, products with high unmet need can be granted an “authorisation temporaire d’utilisation” (ATU)²⁶ prior to receiving a conditional MA approval.

More recently, somewhat comparable schemes have developed in other markets. For example, England’s “early access to medicines scheme” (EAMS). Unlike the French ATU scheme, the company that applies for EAMS must provide the medicine free of charge to

²² For example, global regulatory timelines are changing over time – over the last 10 years. EMA’s have stayed relatively flat (increased a little during the last year) while Japan PMDA, US FDA and China NMPA have dramatically reduced their review timelines over the decade.

²³ It is also possible that where a new indication for an existing product is not (yet) approved or covered, access this may be possible through off-label prescribing.

²⁴ 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.

²⁵ In addition, most countries have named patient compassionate use programs which 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, Olena Efthymiadou, Jennifer Gill, Hana Salyga and Panos Kanavos | November 2021

²⁶ The “cohort ATU” is requested directly by the manufacturer for the use of a single indication in a group of patients, and is currently the preferred option.

the National Health Service (NHS) until the 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. Health Technology Assessment (HTA) guidance, national funding policy, local funding arrangements).²⁷

Early access schemes are not taken into account in the time to availability in W.A.I.T., but the impact of taking into account early access schemes is clear. The time to availability in France is 497 days when one includes products under the ATU system, for which the price negotiation process is usually longer. If one considers that products under the ATU system are directly available (time to availability = 0), the average time to availability is 240 days.

1.5.2. Delay between marketing authorisation and application for reimbursement

Once a medicine has a marketing authorisation, there can still be a delay before the start of the reimbursement process. This can be because some countries want to wait for the formal EMA decision and/or reimbursement decisions in other countries before they start their own reimbursement processes. Even after this, 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 timeline for member states to make P&R decisions, in practice this may be much longer due to clock stops or a lack of adherence.

Initiation of the process

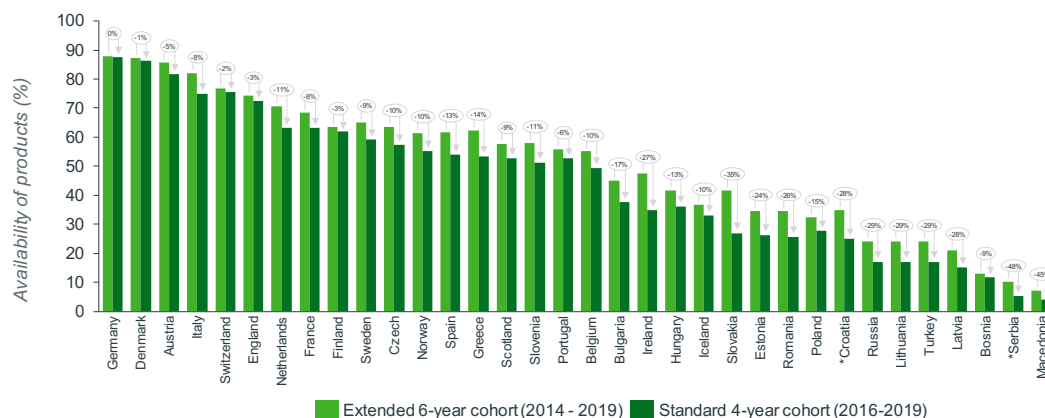
In some markets, there is immediate access after marketing authorisation, at least for some products. For example, in Germany the standard process provides manufacturers with a temporary period of free pricing that enables access to a medicine that has been authorised by the EMA, almost from day one,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

However, in many markets the P&R process does not start automatically; this requires a submission by the company or decision by those in the assessment process. This depends on the rules: the process in some countries is possible prior to marketing authorisation, but in others this requires a positive opinion from the EMA Committee for Medicinal Products for Human Use (CHMP), or even a formal decision from the EC or a publication in the Official Journal of the EU before a dossier can be submitted or is assessed. In some cases, countries even await decisions from other countries, whilst in others the national processes can only start when a cohort of other countries have finalised their decisions at national level.²⁸ This is illustrated in the Figure below – here we look at availability of product approved over two time windows - a four and six year window. As expected this shows that higher level of availability over a longer window with the biggest difference observed for countries that require the product to be launched in a basket of countries.

²⁷ 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>.

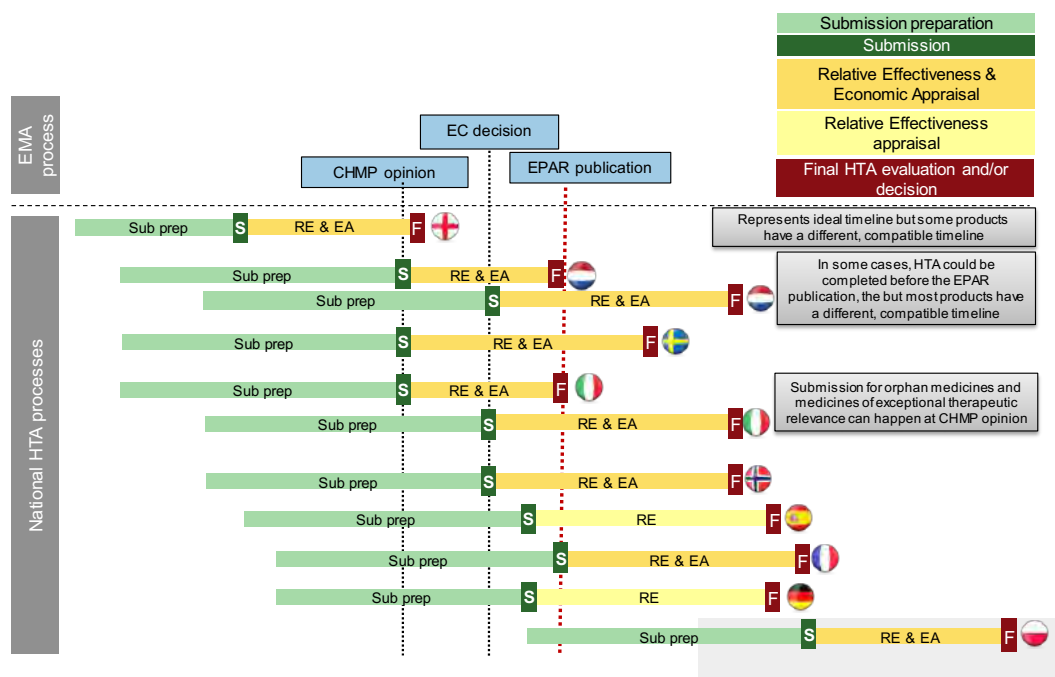
²⁸ For example, in Czechia, as maximal pricing and reimbursement levels are based on referencing to other EU countries, the availability on at least three EU member states' markets is necessary for P&R application. EFPIA Market Launch and Withdrawal Survey. In Bulgaria, manufacturers can submit their dossier to undergo HTA only when a positive recommendation has been issued by the UK, France, Germany or Sweden (Malinowski et al. 2020).

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Figure 10: A comparison of availability over a four and six year window

Source: IQVIA - †In most countries availability equates to granting of access to the reimbursement list, except in DK, FI, NO, SE some hospital products are not covered by the general reimbursement scheme. *Countries with asterisks did not complete a full dataset and therefore availability may be unrepresentative.

In other cases the process is dependent on other stakeholders. For example, in Estonia, applications to the inpatient service list are made by clinicians; therefore, manufacturers are in principle not able to influence this process.²⁹ The different times to submission are illustrated in the figure below.

Figure 11: Time until initiation of the reimbursement process

Source: EFPIA; EPAR refers to European public assessment report

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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

This shows that in some countries the process can start significantly before the marketing authorisation (England), whilst in others there is a delay even after publication in the EU Journal. Leaving to one side the impact of national rules, two other factors need to be taken into account.

A significant amount of research has been undertaken to understand the degree to which delayed application is caused by external reference pricing. The intuition for this is clear: if a country references the price of medicines in much lower income countries, able to pay a much lower price, companies will be encouraged to launch medicines in the high price country first. This will avoid lower prices cascading from one country to another. A series of reports for the Commission have documented this effect.³⁰

Equally, the application for P&R is a time-consuming process. Every country requires the development of a tailor-made dossier in local language and compliance with local rules. Although companies often have specialised groups to manage this process, it is still necessary to prioritise internal activities. This issue is exacerbated for smaller companies that have not gone through the process before and companies that have not launched a new medicine for some time (as shown in the Figure below where larger companies have higher levels of availability). As with any commercial decision, and applicable to many sectors of industrial production, we would expect companies to take into account the commercial size of the opportunity to determine where to put their resources. This is not just about industry resources; HTA bodies do not have limitless capacity.³¹ For that reason, companies are often inclined to not start an application until authorisation to enter the European market has been confirmed.

Figure 12: Percentage of products available in EU countries, segmented by company size

³⁰ 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>

³¹ 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

Sorted by total availability % according to EFPIA W.A.I.T. (2017 – 2020 cohort)

Country	Top-20 global pharma N=76	Other biotech and SME companies N=85	Large company delta % above or below the country average reported in W.A.I.T.
Germany	97%	85%	7%
Denmark	92%	67%	13%
Austria	89%	67%	12%
Italy	88%	68%	11%
Switzerland	88%	59%	15%
Netherlands	91%	48%	22%
England	76%	58%	10%
France	71%	59%	6%
Sweden	83%	40%	23%
Finland	79%	35%	23%
Scotland	67%	44%	12%
Czech	79%	32%	25%
Belgium	79%	29%	26%
Spain	68%	38%	16%
Norway	72%	31%	22%
Portugal	67%	35%	17%
Greece	67%	31%	19%
Slovenia	70%	27%	23%
Luxembourg	66%	29%	19%
Ireland	61%	25%	19%
Hungary	64%	18%	25%
Bulgaria	47%	14%	18%
Cyprus	54%	5%	26%
Iceland	42%	11%	17%
Poland	39%	13%	14%
Estonia	41%	11%	16%
Romania	34%	14%	11%
Croatia	41%	5%	19%
Slovakia	29%	15%	7%
Russia	37%	7%	16%
Latvia	30%	6%	13%
Lithuania	30%	5%	13%
Turkey	21%	8%	7%
Serbia	20%	2%	9%
Bosnia and Herz.	18%	1%	9%
Macedonia	14%	0%	8%
Malta	7%	7%	0%
Kazakhstan	9%	4%	3%
Albania	5%	1%	2%

Source: EFPIA Patients W.A.I.T. Indicator 2021, IQVIA analysis of company size, top-20 pharma defined by 2022 Q1 MAT total sales (Rx only) globally

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 unpredictability of timelines.

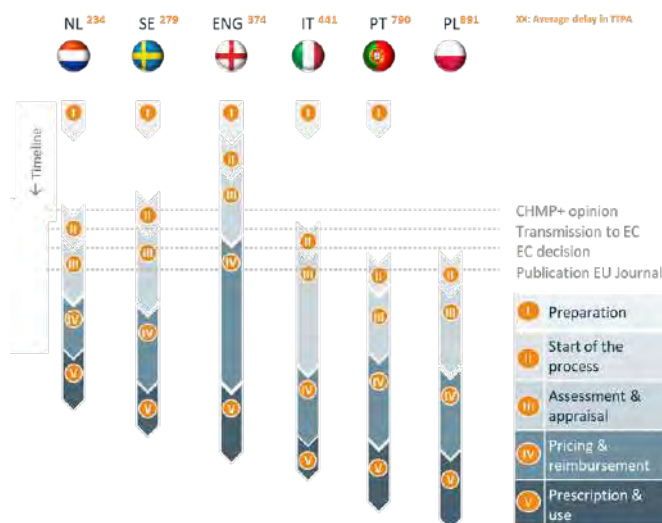
The length of time taken should reflect the EU Transparency Directive (European Commission, 1988). The purpose of this directive is to ensure the transparency of measures that regulate P&R of medicinal products. It sets a strict maximum time of 180 days for reaching a national P&R. This timeline starts from the moment a dossier is submitted and excludes time needed by companies to provide additional information (“clock stops”). The Transparency Directive puts the responsibility in the hands of national governments, whereas it is a responsibility of all stakeholders to allow for reasonable interactions in order to ensure evidence-based decision-making within this time frame.

The length of time taken from application for reimbursement to approval for reimbursement clearly varies significantly across EU countries (after taking into account the delay initiation of the process). This is consistent with the OECD analysis, which was able to separate these time periods for a selection of European countries.

There is relatively little data on the time taken from the start of the national P&R process to its conclusion. The data from the TPA study for the six case study countries is below. This

shows that even after taking into account delayed initiation, there are significant differences across countries.

Figure 13: Start of the national process in the six case study countries



Source: Time to Patient Access

It has also been pointed out by a number of different authors that tailored approaches for different types of medicines can improve access.

- In some markets there is immediate access of medicines that are dispensed in the hospital, but the national reimbursement process applies 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.³²
- In other cases there are different channels for different types of medicine. For example, Deticek found that the most successful countries in terms of rapid availability of orphan medicines were Germany, Norway, Finland, Sweden, and France. These countries also have specific mechanisms to improve patient access to these medicines and to grant full or substantial reimbursement from public resources.³³

1.5.3. Delays due to the value assessment process

A part of the P&R process is the value assessment process. Misalignment on evidence is reported as one of the most prominent and complex delaying factors. Misalignment takes place not only between industry, regulators, and HTA bodies, but also occurs between regulators and HTA bodies, as well as among different HTA bodies. Misalignment can be found in all assessment criteria including patient population, comparators, trial design, end points, and statistical analysis. Even once there is agreement on evidence, there can be a

³² How is patient access to high-cost orphan drugs changing? <https://www.remapconsulting.com/patient-access-to-high-cost-orphan-drugs-remap-consulting/>

³³ Patient Access to Medicines for Rare Diseases in European Countries. Andreja Detiček, Igor Locatelli, Mitja Kos

significant debate on whether this justifies the price of the medicine. Finally, different countries have adopted different approaches to class competition and the value of choice.

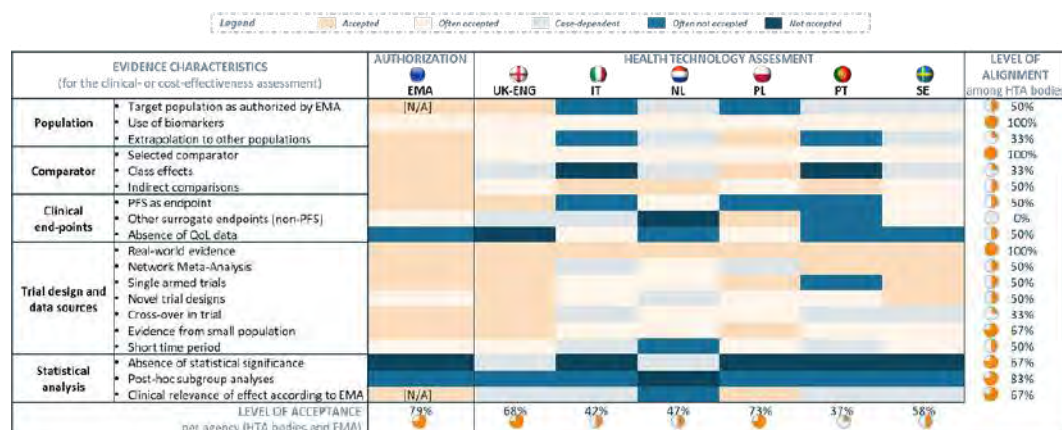
Misalignment on evidence requirement

Once the P&R process is initiated, one of the reasons that the national timeline gets extended are clock stops, requests for information or rejections during the HTA process. Different countries have different requirements for the evidence, during the assessment process, and this represents a challenge, as (1) evidence is developed at a global level and hence developing additional country specific evidence can be time-consuming, and (2) the evidence requirements are not always predictable (even with early dialogue processes that have developed in Europe over the last five years).

To illustrate the differences in evidence requirements we can compare the evidence requirements of EMA and the HTA bodies in the six case study countries from the TPA project (see Figure 12). Based on desk research and interviews with agency representatives, for each agency the research assessed whether 19 different characteristics would be accepted as convincing evidence.

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

Figure 14: Evidence requirements vary between agencies, prolonging national discussions and decision-making.



Source: Time to Patient Access

This is illustrated in the figure above. The grey colour code reflects acceptance on a case-by-case basis. The blue colour code (“often not accepted”) and lighter orange colour (“often accepted”) also reflect a certain level of unpredictability.

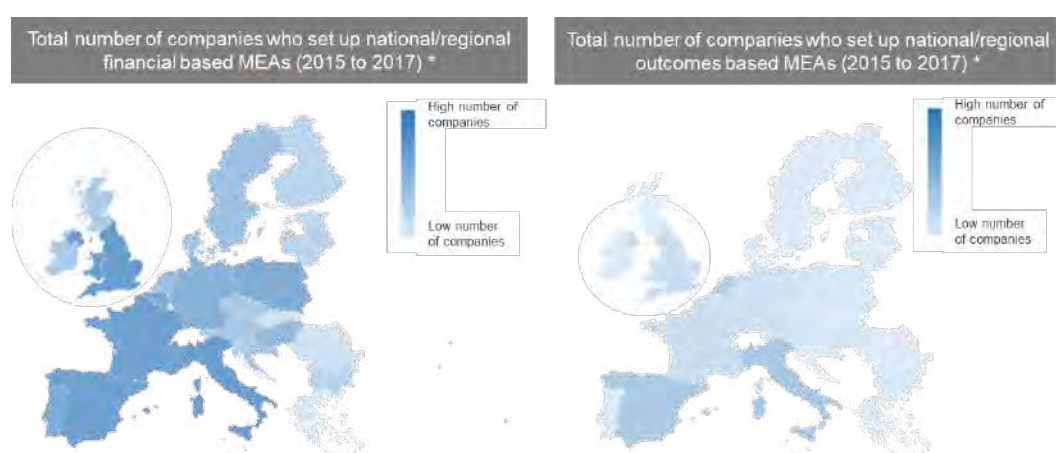
Misalignment of value and price

Next, even if there is agreement on the evidence regarding the value of a medicine, different 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.

There is clearly also a debate around delays and price. Looking at a simple correlation we find that there is a positive relationship between price indices and availability. This is, however, too simplistic, as high price countries may have quicker diffusion and greater usage. So there are many confounding factors. The limited number of studies that have tried to unpick the relationship between delay and price have not found a meaningful result. Ferrario (2018) found expected prices do not affect the speed of launch although pointed out this may be due to limited variation in prices across the four study countries.³⁴

However, there is broad consensus that prices need to reflect the ability to pay. Where prices are higher than the perceived value or affordability, there is an inevitable delay as the price is negotiated. This is clearly complicated by external reference pricing (discussed above); this means that the agreed price needs to take into account how this price will be used outside of the country, in addition to whether it aligns with the assessment of value by the national HTA body. Where it is possible to use flexible contracts to align price and value, this should reduce delays. However, the ability to agree novel payment mechanisms varies considerably around Europe. This is particularly the case in Central and Eastern Europe, where we observe the largest delays.

Figure 15: 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 a particular medicine also varies. Countries may have different numbers of patients with a particular condition (some countries may have very few); and approaches to treatment may vary, with some countries favouring surgical approaches rather than therapeutic interventions. So clinical and epidemiological factors affect the degree to which countries have an unmet need and therefore the degree to which these are prioritised in P&R process and value assessments.

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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

There is another dimension to this and it is about physician choice and the value of competing medicines. Different countries take different approaches as to value of class competitors. Some countries believe that physicians should have access to all the products on the market, in order to provide patients with the best products for them and to allow physicians clinical freedom. Equally, competition between innovative medicines is encouraged in some markets, with the follow-on products in a class being encouraged as this can lead to competition and better value for the payer. Other countries have favoured an 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. If this is the case, is it unsurprising that we see access to only a subset of the products. To examine this, IQVIA has examined a series of ATC4 therapeutic classes. It is not surprising that as the number of ATC4 options decreases, more countries approve all authorised options.

Given that the number of options vary in different ATC4 classes, we would therefore expect to see differences in availability of products. This is validated by the evidence. If we look at HIV antivirals (J5C9). Although availability varies significantly across the European countries, all countries have access to at least one product in the class.

Figure 16: Number of products available in a therapeutic class (the example of HIV antivirals (J5C9))



Source: EFPIA Patients W.A.I.T. Indicator 2021 IQVIA ATC4 class (J5C9, HIV antiretrovirals, n=8) size,

A similar result is seen in other therapeutic areas: Hep-C, PD-L1, and Her-2 inhibitors.

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 readiness

The fourth category of root causes relates to the health system, its funding and infrastructure. To understand availability and delay we need to take into account health system readiness, particularly insufficient budget to implement decisions, and the infrastructure for diagnosis.

Insufficient budget to implement decisions

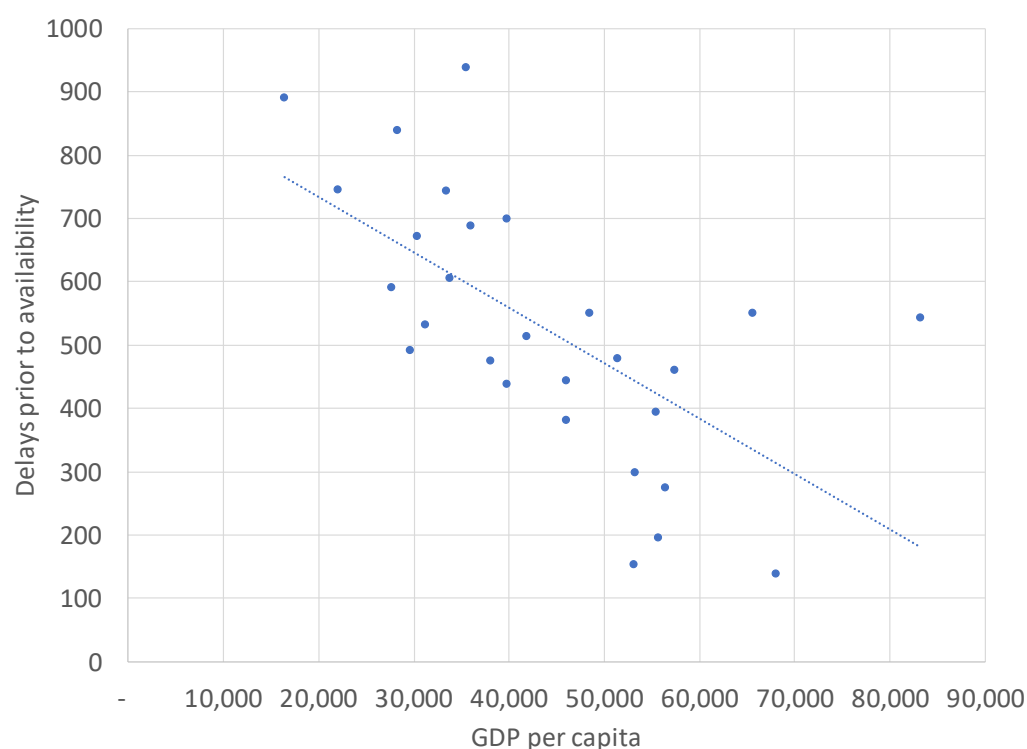
Within Europe, we clearly have countries with very different levels of income, with GDP per capita varying from €16,000 to €80,000 per annum. They also have made different decisions regarding the amount that they invest in healthcare. The data from the OECD clearly shows the European differences in economic context:

- Relative healthcare spending as a % of overall GDP is more than twice as high in France or Switzerland (11.3% and 12.4% respectively) as in Romania (5.2%).

- Relative pharmaceutical expenditures as a % of overall GDP is 3.5 as high in Greece and over 5 times as high in Bulgaria (2.2% and 3.3%, respectively) compared to Luxembourg (0.62%).
- Absolute healthcare spending ranges from €6,600 per capita in Switzerland respectively to €1,300 per capita in Romania (OECD, 2020).

Given the difference in income and spending on healthcare and medicines, it is unsurprising that the prioritisation of health technologies varies across European countries. Given healthcare priorities funding, it would be surprising if we saw the same access to different forms of healthcare.

Figure 17: Relationship between time to availability (delays) and GDP per capita



Source: IQVIA

As shown in the figure above, we do find a negative relationship between income and delays (although there are clearly many other factors as well). This result is consistent with the broader economic literature. Indeed, there are many papers showing that the impact of the size of the market remains, even after taking into account many other factors. For example, Costa-Font (2015) observed a significant and robust market size effect that decreases the launch time of new pharmaceutical products as market size increases.³⁵

Diagnosis, supporting infrastructure and relevance to patients

The existing health infrastructure is a barrier to access in many European countries. For that reason, even after reimbursement, healthcare systems may face difficulties absorbing

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

and using a new therapy in the most optimal way due to the need for high quality health facilities, diagnostic centres and health personnel.

In reality, there are many barriers in the infrastructure that mean applying for reimbursement for a medicine in some markets is not realistic. This is particularly true for highly specialised or orphan medicines:

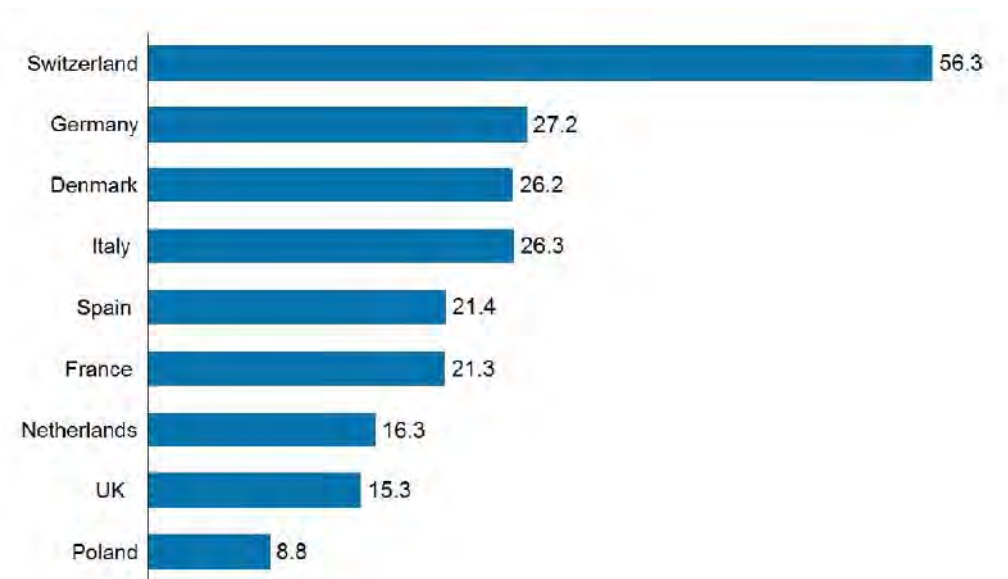
- Accurate and timely diagnosis is dependent on the availability of accessible screening and diagnosis programs and services, which itself depends on the infrastructure and expertise (e.g. number of geneticists) available.³⁶ The degree to which countries have adopted widespread screening or targeted diagnosis of at-risk patients varies significantly.
- Even where diagnosis programs exists in a country, access to diagnostic testing can be limited. There is a need for appropriate reimbursement for (newly approved) diagnostics.
- Diagnosis requires investment in reimbursement of diagnostics and appropriate investment in testing facilities, but also requires investment in physician education (and a focus on paediatricians) and an effective referral process.
- Given the small number of patients needing highly specialised or orphan medicine, it is best to concentrate expertise in Centres of Excellence (CoEs), but these are not evenly developed across European markets.

For many countries the availability of scientifically robust epidemiological data for individual rare diseases varies greatly, if it is available at all.³⁷ This can create a vicious cycle where the lack of epidemiological country specific data contributes to a lack of appropriate health resource prioritisation decisions, and little attention being given to the need to develop rare disease diagnosis programs. The lack of a developed coding nomenclature for rare diseases also creates challenges, particularly for healthcare systems to map out their specialised healthcare services and budget impact.³⁸

As a result – given that the number of patients for rare diseases may be very low, and finding these patients may be difficult – ensuring appropriate use and pharmacovigilance is challenging and the commercial viability of applying for reimbursement does not currently exist.

Figure 18: Investment in in vitro diagnostics (per capita expenditure on in vitro diagnostics (€) (2016))

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- 36 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
- 37 Manuel Posada De La Paz, Domenica Taruscio, Stephen C. Groft (2017). *Rare Diseases Epidemiology: Update and Overview*. Springer International Publishing (Verlag)
- 38 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



Source: EBE Personalised Medicine Report

Given this, it is unsurprising that for some orphan medicines the availability across Europe is unfortunately low. 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 on the use of compassionate use programmes across Europe.³⁹

1.5.5. Delay from national to regional approval

Most of the 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 need to be made at all levels from national level to regional level and to then local hospital level, thus prolonging the time before patients can access treatments.

Multiple layers of 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. Other countries organise these decisions partly at a national level and partly at a 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 different health insurers) or on a hospital level (WHO, 2018).

To illustrate this, many papers examine the situation in Italy. For example, a recent paper found that for the regional access, both the timing and the number of drugs available for patients were widely different from region to region. The mean best regional time (defined as the average number of days after AIFA market authorisation as published in the GU and the first purchase date in the first Italian region) was 29 days. The longest regional time (the number of days between GU and the first purchase in the last region for which data

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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

are available to date (July 2016)) was 293 days.⁴⁰ More recent analysis has shown that there has been little improvement over the last five years. Even when a national price applicable across all the regions is agreed, a medicine still has to go through 20 different processes locally from Lombardy in the north to Sicily in the south before it is available to patients. This can take anywhere from 6 to 9 months depending which region the patient lives in. Although the academic literature has focused on Italy, this applies to many markets in Europe.

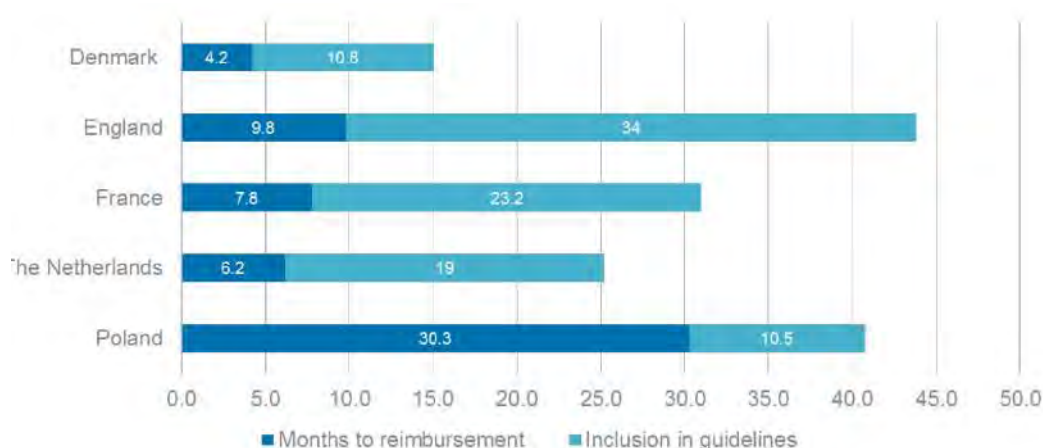
1.6. Availability is not access

Even once a medicine is on the public reimbursement list and has navigated any regional process, this does not mean that patients have access to medicines. The TPA project identified remarkable differences in the use of new oncology therapies once reimbursement is in place. Based on an assessment on access in sixteen countries, twelve months after reimbursement, for thirteen recently launched therapies, the average access ranged from 61% to 0.3%.

There are many additional barriers that affect usage of medicines:

1. An additional delay on top of the P&R period is attributed to the time between the P&R decision and the publication in the national gazette (journal). For example, this is necessary for final access in Belgium, adding an additional level of bureaucracy and a delay of two to three months.
- Clinical guidelines do not always include the most recent therapeutic innovations. The absence of clinical guidelines has the potential to lead to 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 hold back from starting 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.

Figure 19: Average access timeline for personalised oncology medicines

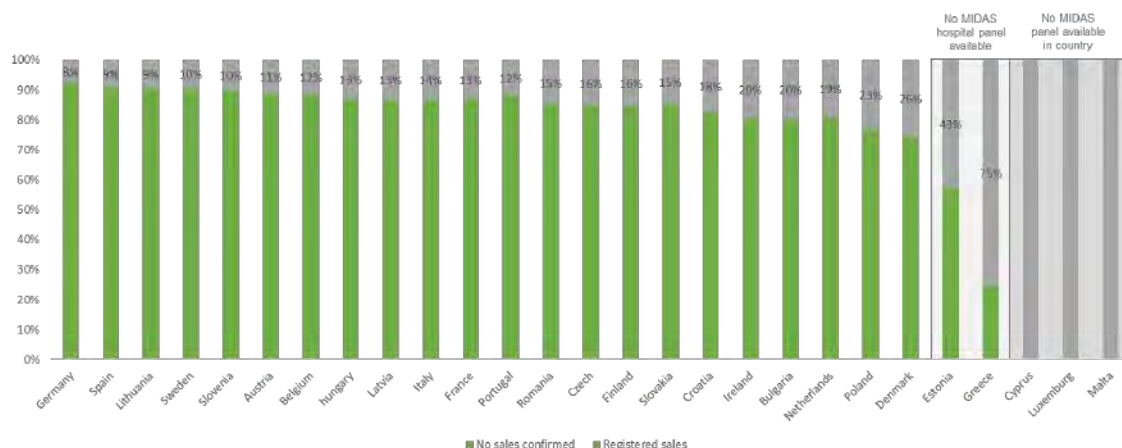


Source: EBE Personalised Medicine Report

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 is complete 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 74% of the products that are available in Romania (see Figure 18). Given this experience, it is not surprising that not all companies choose to apply for reimbursement in these markets.

Figure 20: Percentage of available products with no recorded sales in the EU



Source: The Patient W.A.I.T. Indicator 2021; IQVIA MIDAS 2015 - 2022; Analysis includes all products which have both availability in EU and show EU sales in MIDAS. 'No sales' is defined as no sales found in IQVIA MIDAS data since 2015. Some countries in this analysis are not covered by IQVIA data, or do not cover the hospital channel (coverage is retail only).

1.7. The impact of delayed access to innovative medicines

Although there are many statistics on the percentage of medicines available or the length of time taken for a medicine to be made available, the real impact of delays is on patients, the healthcare system and society. It is difficult to quantify the impact of delays but there is no doubt this leads to:⁴¹

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

The scale of the potential impact of reduced delays can be illustrated by looking at potential efficiencies. For example, recent analysis has estimated the potential to reduce the length of time between CHMP opinion and EC decision. If this could be reduced by 12 days this would lead to 3,300 years of potential lives (YPL) saved. If this was increased to a 15-day reduction this would increase saving to 4,200 YPL.⁴²

⁴¹ 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/>

⁴² Vintura, November 2021, Every Day Counts, Improving Regulatory Timelines to Optimise Patient Access to Innovative Oncology Therapies in Europe

1.8. Policy solutions to improve availability of innovative medicines

It is clear from this paper that the reasons behind the unavailability of medicines and delays are multifactorial. These are rooted in the medicines access systems and processes in the member states and the corresponding impact on commercial decision-making. These include a slow regulatory process, late initiation of market access assessment, duplicative evidence requirements, reimbursement delays, and local formulary decisions. It is also clear that there is a shared aspiration to “make sure that patients across Europe have new medicines and therapies in their countries quickly”.⁴³ As the root causes are multifactorial, they can only be solved by different stakeholders working together. To bring different stakeholders together to discuss the root causes, consider different policy solutions and how these could work in practice, EFPIA has called for a High-Level Multi-Stakeholder Forum on Access to Innovation and made a series of commitments. This includes a commitment to file pricing and reimbursement applications in all EU countries no later than 2 years after EU market authorisation. This commitment reflects the joint ambition of industry and society to make innovation for unmet health needs available for patients and health systems across Europe as soon as possible. However, no single commitment will address unavailability and delay and this needs to be part of a package of policy proposals.

Reflecting the different root causes, there are five areas where proposals are required:

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

There is shared aspiration to reduce regulatory approval times in Europe and bring these in line with international best practice.⁴⁴ There are several areas for action within the existing legislative framework to address this: encourage the use of new types of clinical trials; allow greater use of data from real-world use; allow ongoing dialogue between the developer and the regulator about a treatment throughout 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. The evaluation and the revision of the basic pharmaceutical legislation (Dir 2001/83 and Reg 726/2004) will provide further opportunities and should reinforce expertise-driven assessment and enable a more agile centralised authorisation framework by removal of unnecessary interfaces between European Commission, European Medicines Agency (EMA) and Committees (Member States representatives); enhance the expedited pathways framework; expand the role of EMA in the assessment of drug-device/diagnostic combination products and replace the paper patient information leaflets with electronic versions.

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

⁴³ As set out in the European Commission's Pharmaceutical Strategy Roadmap - <https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12421-Pharmaceutical-Strategy-Timely-patient-access-to-affordable-medicines>

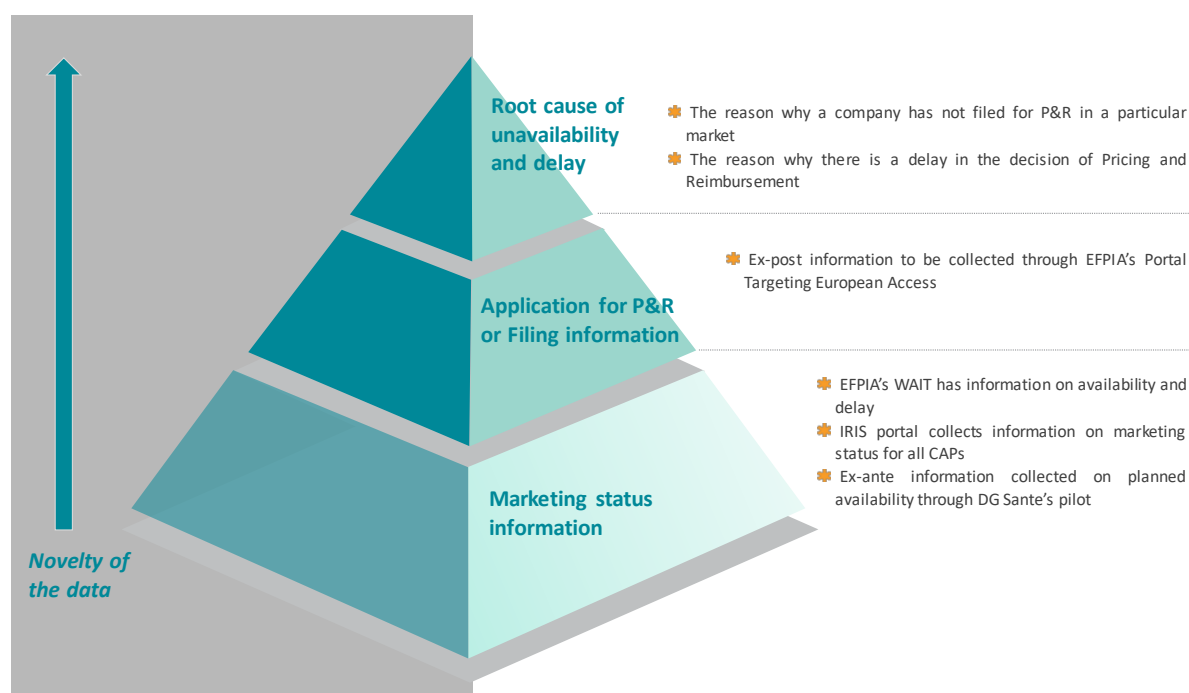
⁴⁴ Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and The Committee of the Regions, Pharmaceutical Strategy for Europe COM/2020/761 final

The industry have committed to the creation of a portal where marketing authorisation holders (MAH) can provide timely information regarding the timing and processing of pricing and reimbursement (P&R) applications in the various EU-27 countries, including the reasons why there is a delay in the P&R decision or why the MAH has not filed in a particular market.

EFPIA already contributes to transparency on unavailability and delay with its yearly published Patients WAIT report, highlighting the delays to patient access across the EU, as well as this current 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 committed to the development of a European Access Portal.

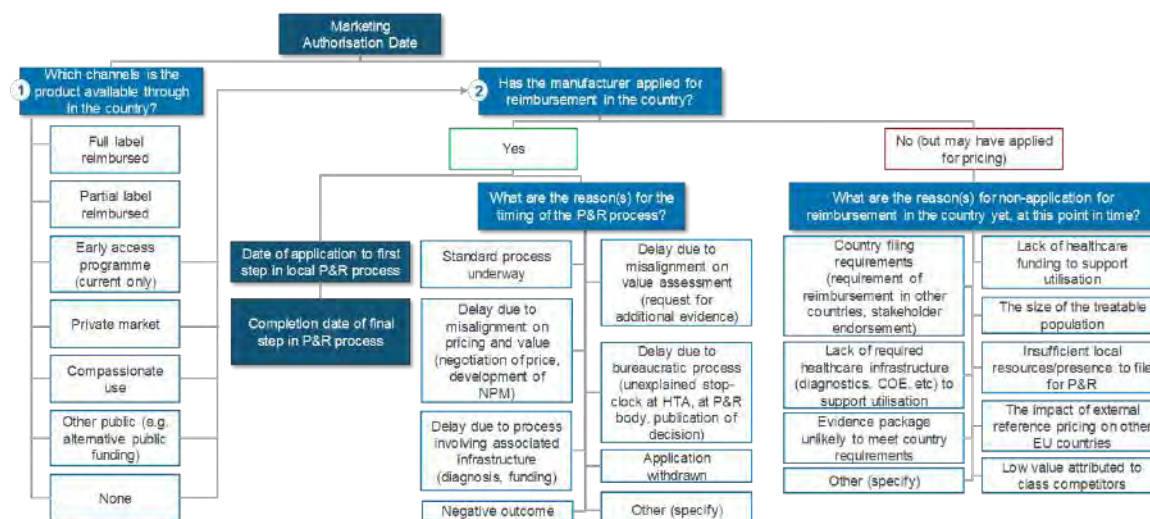
Marketing authorisation holders of centrally approved product will be requested to provide timely information regarding the timing and processing of P&R applications in the various EU-27 countries including the reasons why there is a delay in the P&R decision or why the MAH has not filed for P&R in a particular market.

Figure 21: Potential for more granular data on unavailability and delay



The role of the Portal is to improve transparency regarding the root causes of unavailability and delay, including the role of the environment. It would add new information to the debate on the filing for pricing and reimbursement and the reasons why we see no application for reimbursement or a delayed process allowing the root causes of unavailability to be recognised.

Figure 22: Data captured by the Portal



This will allow data on delay and lack of availability to be put into context and support the broader understanding that it is a shared responsibility, requiring a shared solution.

Aggregate data collected on timing of filing/no filing and root causes of individual products will be disclosed through a regular report that tracks progress in lowering the hurdles causing unavailability and delay.

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 payment and pricing models**. 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, whilst providing sufficient incentives for innovation.^{45,46}

Although there are examples of novel pricing and payment models 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 whilst 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.

⁴⁵ <https://efpia.eu/media/554543/novel-pricing-and-payment-models-new-solutions-to-improve-patient-access-300630.pdf>

⁴⁶ <https://www.efpia.eu/media/602581/principles-on-the-transparency-of-evidencefrom-novel-pricing-and-payment-models.pdf>

April 2022

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), while retaining confidentiality of commercial terms.
5. **Infrastructure Principle:** Stakeholders should work together to ensure the required data infrastructure is fit for purpose and legal frameworks are in place to enable

The industry has an important role to play and commit to an open dialogue and collaboration with payers and policy makers to reach a win-win solution putting patients' interest first. the use of the different novel pricing and payment models.

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 is predominantly the same for all markets – such as safety and efficacy data from registration trials. This is because HTA agencies adopt different approaches to rating and interpreting the data. This 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 start of the implementation period, there is an opportunity to establish an efficient system of European assessments of relative efficacy at time of launch but the EU HTA regulation will only deliver against its promise, if all stakeholders collaborate during the next coming years on implementing a future-proof system that delivers high quality outputs that are relevant for decision making in Member States.

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

The industry is committed to participating in a **structured dialogue on conceptual framework for Equity-Based Tiered Pricing (EBTP)**. The objective is 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.

Building on Value Based Pricing (VBP), as the foundation for pricing innovative medicines (where the pricing medicines is based on the value they deliver to patients, healthcare systems and society), Equity Based Tiered Pricing (EBTP) is a framework for the pricing of medicines that takes into account a country's ability to pay with the objectives of improving patient access (defined broadly in terms of speed and availability) across Europe. The commitment of both Member States and industry is needed for EBTP to work in practice, and some of the current barriers to access and differential pricing need to also be addressed. This includes addressing how External Reference Pricing (ERP) is used and ensuring that non-extraterritoriality is observed. EFPIA members support an EBTP approach based on a concrete conceptual framework with the following characteristics:

- To promote faster and greater access, companies would voluntarily commit to applying EBTP principles to specific innovative medicines.

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- The framework would include simple rules regarding the tiers and how this affects the price of medicines when EBTP is applied, but would leave room for individual companies to determine how this is applied.
- In order for prices to reflect value and be consistent with EBTP, companies will continue to negotiate with individual countries in order for prices to reflect the value that medicines deliver in that market. EBTP would set a framework for prices but the final price is dependent on company strategy and negotiations in the Member States. EBTP does not replace value assessment or value-based pricing.
- The resulting price must be commercially confidential. Given the need for price confidentiality, it will not be possible to publicly observe exactly how EBTP is working in practice. A process of verification would be required.

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

1.9. Conclusion

The need for a dialogue on how to improve availability and reduce delays is clear. Although it is inevitable that availability will vary to some extent across European markets, patients in one part of Europe should not have to wait seven times 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 on their postcode. The industry has set out a number of commitments demonstrating how the industry can play a key role in addressing the issue of unavailability and delay.

Glossary:

- **Access:** Refers to actual systematic usage of medicines.
- **Availability:** 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 / 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 to be included 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 whether a product is placed on the market for sale (not to its reimbursement by the national or regional authorities).