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

Executive Summary[1]

The unprecedented speed of innovation exhibited over the last five years and the promise of the industry pipeline[2] 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 2020, the average time to reimbursement for innovative treatments across EU and European Economic Area (EEA) countries continues to be as long as 504 days, ranging from 120 days in Germany to over 883 days in Romania. The industry shares concerns about these delays and recognises that delays and the unavailability of medicines harm patients. Moreover, there is a concern that delays could worsen as we consider the on-going consequences of COVID-19.

EFPIA has investigated the root cause of access inequality and found there are 10 interrelated factors that explain unavailability and delays. 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. 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 include:

- Proposals to speed up the regulatory process, delivering safe and high-quality diagnostics, vaccines and treatments to patients as fast as possible
- Proposals that aim to increase transparency of information regarding placing on the market of centrally approved products
- Proposals to facilitate a process that allows prices to align with value and ability to pay

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.

- Proposals to improve the efficiency and quality of value assessment
- Proposals to ensure equity of access and solidarity across EU member states

The present report is an updated version of the report that EFPIA released in June 2020, which was used a basis for discussion with several EU and national policy-makers and stakeholders. The present report takes stock of these discussions and offers a set of policy proposals as possible avenues to 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.[4] However, in recent years, concerns regarding availability and delays have intensified.

- European Commission: The Commission has set out how patients in the European Union (EU) still have different levels of access to medicinal products and do not always access innovative therapies. For example, in the EU Pharmaceutical Strategy the European Commission reported that "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."[5] Indeed, a number of proposals have been considered, including: a stricter interpretation of the sunset clause[6], which could be a basis to compel manufacturers to launch products in more/all EU markets; strengthened Public Service Obligations; and greater transparency on Launch/Withdrawal Intentions. For example, in June 2020, the Commission launched a consultation on the Pharmaceutical Committee's decision to initiate a pilot project on market

4 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/

5 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

6 This refers to Sunset Clause: Article 14 Regulation 726/2004 on the authorisation of medicinal products: §4: any authorisation that is not followed by the actual placing on the Union market within three years shall cease to be valid; §5: when an authorised product previously placed on the market is no longer actually present on the market for three consecutive years, the authorisation shall cease to be valid.

launch intentions of CAPs, which became reality on 25 March 2021 with the formal launch of a pilot whereby marketing authorisation applicants of oncology and orphan medicines are invited to voluntarily share relevant information on their actual market launch plans.

- EURORDIS: In a recent paper on improving availability of medicines, EURORDIS concluded: "We must remember that the majority of people living with a rare disease at this very moment have delayed or no access at all to the medicine they need […]. If a therapy is approved but does not reach those who need it, it has failed in its primary purpose. We need to close the gap between innovation and access, which is primarily due to the discrepancy between authorisation granted at EU level for a market fragmented across 28 different countries."[7]
- Institute of Cancer Research (ICR): ICR set out in a recent report "that drugs are taking longer to reach patients when we would expect the process to be getting quicker. With targeted treatments, it should be possible to run smarter, faster trials and to take a more flexible approach to assessing the results for rapid regulatory approval. We also want to see innovative new drugs become available to patients earlier in the course of their treatment, to give them the best possible chance of benefiting."[8]
- Academia: "There is consensus that to ensure timely patient access, current access processes have to be adapted to keep pace with scientific developments and affordability needs. This will help to ensure that people living in EU countries with access delays and lower levels of economic development are also able to receive quality cost-effective care."[9]

Although these concerns are not new,[10,11,12] the industry shares the concern about these delays and recognises that delays and the unavailability of medicines harm patients, and

7 "Breaking the Access Deadlock to Leave No One Behind" Available at https://www.eurordis.org/sites/default/files/reflexion-paper.pdf

8 https://www.oncology-central.com/subject-area/personalized-medicine-taxonomy/delays-licensing-denying-cancer-patients-access-innovative-treatments/

9 Wilking et al. (2019) 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://esmoopen.bmj.com/content/esmoopen/4/6/e000550.full.pdf

10 EUR Lex (2016) "Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance systems." Available at: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31989L0105. There are rules regarding the length of these processes – the EU Council Directive 89/105/EEC (commonly referred to as the "Transparency Directive") requires, among other transparency provisions, that member states issue a pricing decision within 90 days (if member states decide on price only), set a 90-day limit on reimbursement decisions (if member states decide on reimbursement only), and set a 180-day limit for joint P&R decisions.

11 Ades, F., Zardavas, D., Senterre, C., de Azambuja, E., Eniu, A., Popescu, R., Piccart, M. and Parent, F. (2014) "Hurdles and delays in access to anticancer drugs in Europe," ecancermedicalscience, 8:482.

12 European Cancer Patient Coalition (2015) "Challenging the Europe of Disparities in Cancer." Available at: http://www.ecpc.org/Documents/Policy&Advocacy/Europe%20of%20Disparities/Europe%20of%20Disparities%2027th%20Sept%202015.pdf

that stakeholders should work together to reduce these. This is likely to be even more important in the post-COVID debate on policies affecting the access environment for innovative medicines. To contribute to this debate, EFPIA has commissioned a series of workstreams to investigate the root causes of unavailability and delay:

- The EFPIA Oncology Platform supported an initiative named Time to Patient Access (TPA), which brings together diverse stakeholders across Europe to jointly identify factors which cause access delays, and co-create solutions that could accelerate time to patient access.[13,14]
- A series of specific analyses based on the most recent W.A.I.T. data from IQVIA. This includes looking at the delays in different therapeutic areas and the correlation between delays and types of company.

The purpose of this paper is to set out 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):

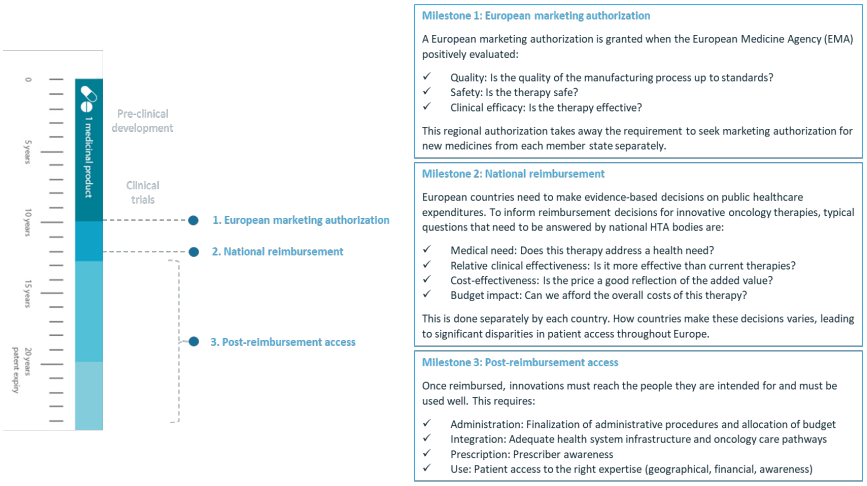
- A European marketing authorisation needs to be granted, confirming the quality, safety and efficacy of the therapy.
- Authorities within countries have to secure national (and regional) reimbursement of the therapy under an insurance or reimbursement scheme, in order to secure the adequate provision 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 – so we focus on the first two milestones.

13 https://www.efpia.eu/media/578013/every-day-counts.pdf. This is based on case studies conducted in six European countries, which together represent the diverse access contexts in Europe. Countries selected were England, Italy, the Netherlands, Poland, Portugal and Sweden.

14 https://www.efpia.eu/news-events/the-efpia-view/blog-articles/everyday-counts-9-reasons-why-patients-wait-longer-to-get-access-to-new-cancer-medicines/

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

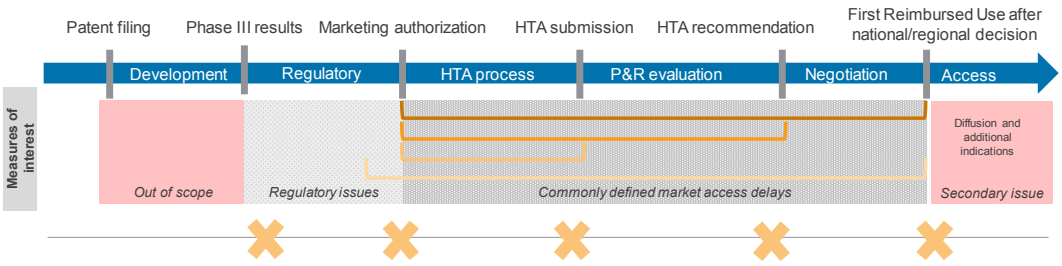


Source: EFPIA

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

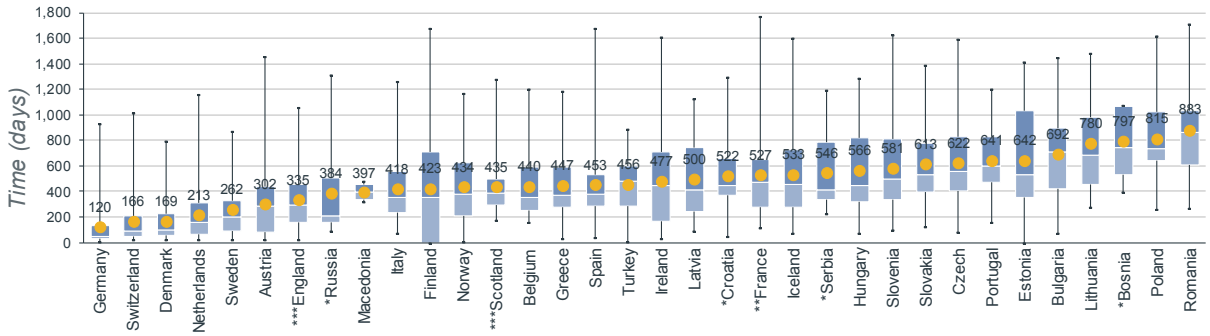


Source: EFPIA

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 504 days, ranging from 120 days in Germany to over 883 days in Romania.

Figure 3: Median time to availability in days (2016–2019) [15]



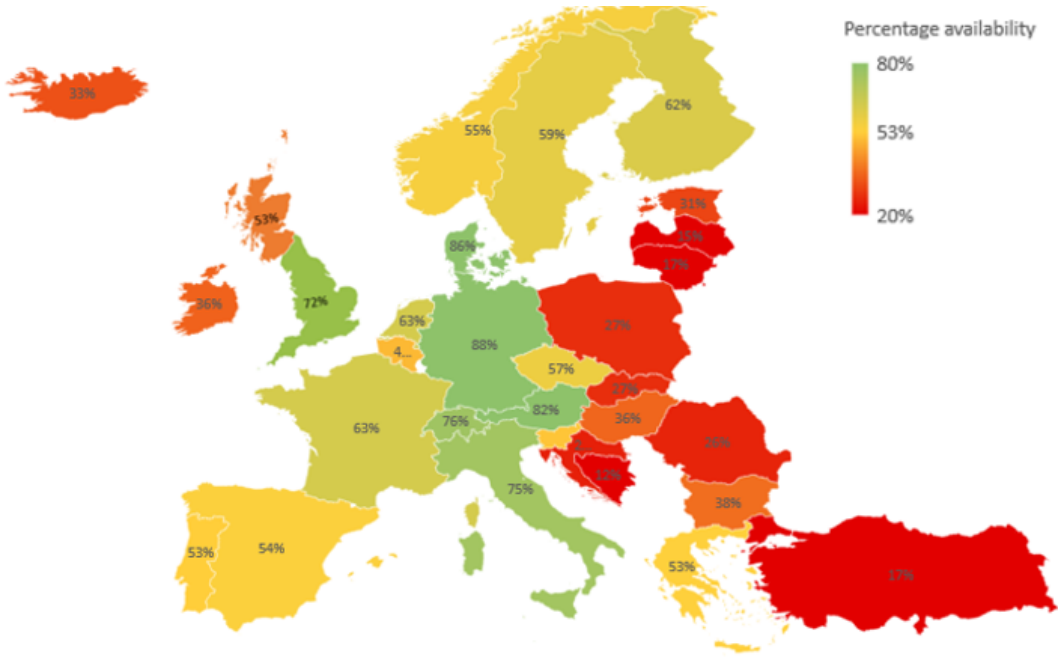
Source: The Patient W.A.I.T. Indicator 2020

Patients in different countries can wait more than seven times longer than patients in other countries to get access to the same medicine.[16] 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.

15 European Union average: 504 days (mean %) (excludes data from Cyprus, Malta, and Luxembourg as these countries are not included in the study) †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. **For France, the time to availability (527 days, n=86 dates submitted) 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 257 days. For products which do not benefit from ATU system (n=48 dates submitted), the average delay is 488 days. ***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.

16 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/

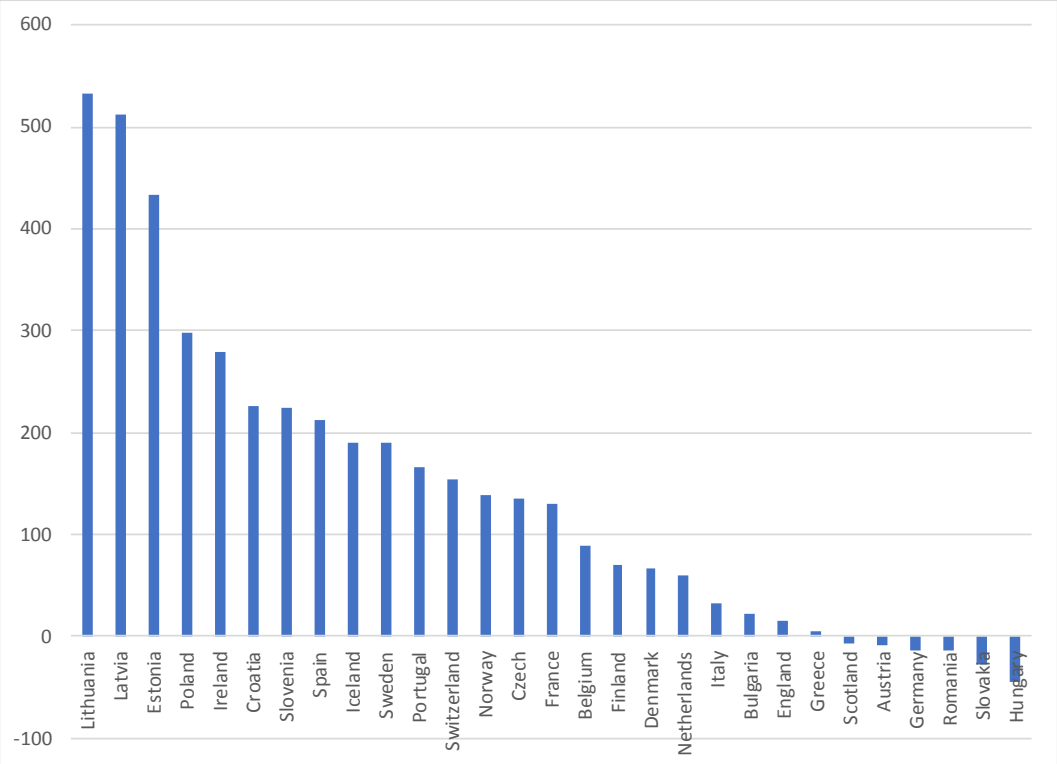
Figure 4: Comparing access across European countries



Source: The Patient W.A.I.T. Indicator 2020

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 (2016 – 2019) – positive means orphan are slower than all medicines by number of days



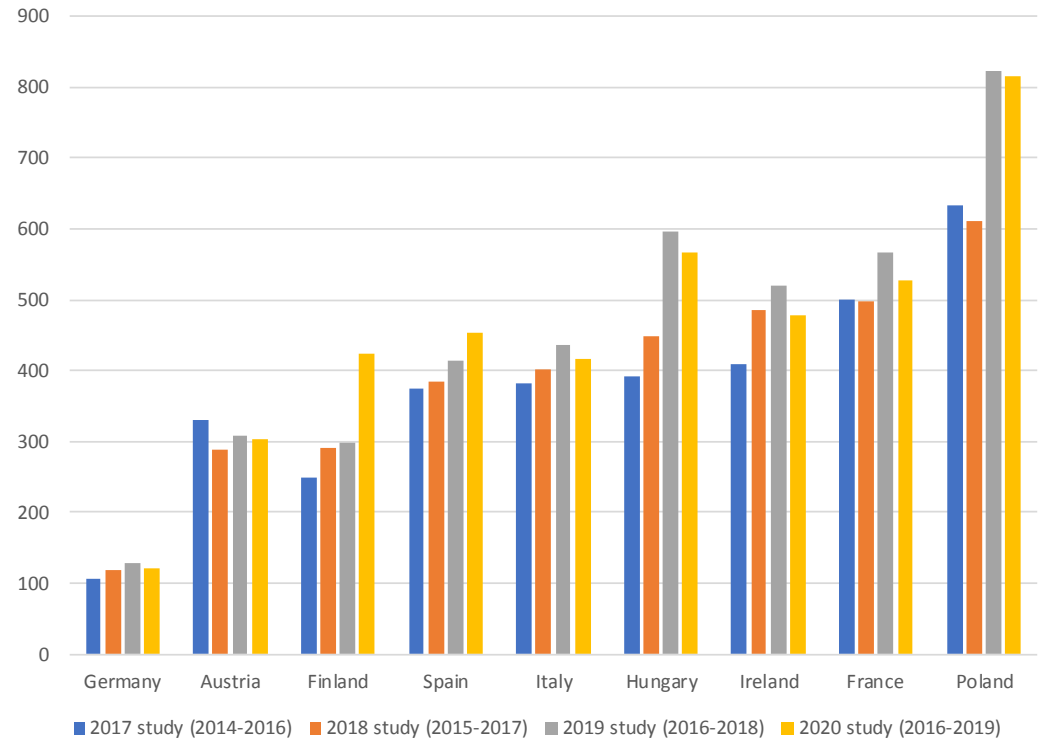
Source: The Patient W.A.I.T. Indicator 2020

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.[17] This is likely to become an even bigger concern as we consider the consequences of COVID-19.

17 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 Patient W.A.I.T. Indicator 2020

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.[18] 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 untease 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.”[19]

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.

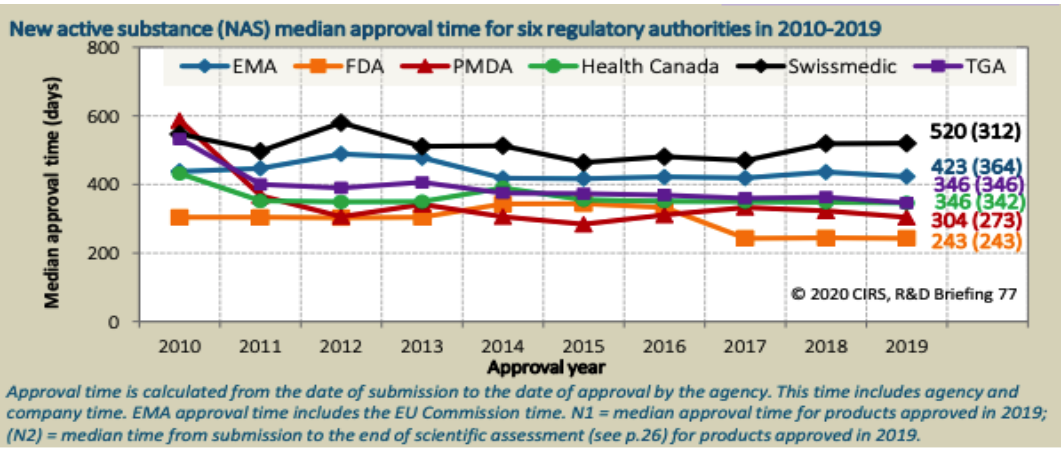
18 Greece: article 22 of Law 4633/2019: medicines with patent protection are subject to health technology assessment (HTA) in Greece only if they are reimbursed in 5 other countries with HTA process from the following list: Austria, Belgium, France, Germany, Denmark, Spain, Netherlands, Italy, Portugal,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

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

The speed of regulatory process

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).

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



Source: https://cirsci.org/wp-content/uploads/2020/06/CIRS-RD-Briefing-77-6-agencies.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).[20]
- 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).[21] 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 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.[22] Submissions to the FDA were also made on average 12.9 and

20 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

21 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

22 Cross-comparison of cancer drug approvals at three international regulatory agencies. Samuel, N. and Verma, S. *Current Oncology* 23(5): 454–460

28.4 months earlier than submissions to Health Canada and to the EMA, respectively.

- A more recent paper found the overall median approval time for anticancer drugs and immunomodulators varied across six major regulatory agencies in the EU, the US, Japan, Canada, Switzerland, and Australia, from 240 days (FDA) to 423 days (EMA and Swissmedic) in 2014–2018.[23]
- 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.[24]
- 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.[25]

For other categories of medicine, the difference may be smaller but the FDA is still faster than the EMA.[26]

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.[27] 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.[28,29] 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.

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23 The Centre for Innovation in Regulatory Science (CIRS), 2019

24 Regulatory Review of New Therapeutic Agents — FDA versus EMA, 2011–2015 https://www.nejm.org/doi/full/10.1056/NEJMc1700103#t=article

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

26 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).

27 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.

28 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.

29 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.

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)[30] 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 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).[31]

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 527 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 257 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.

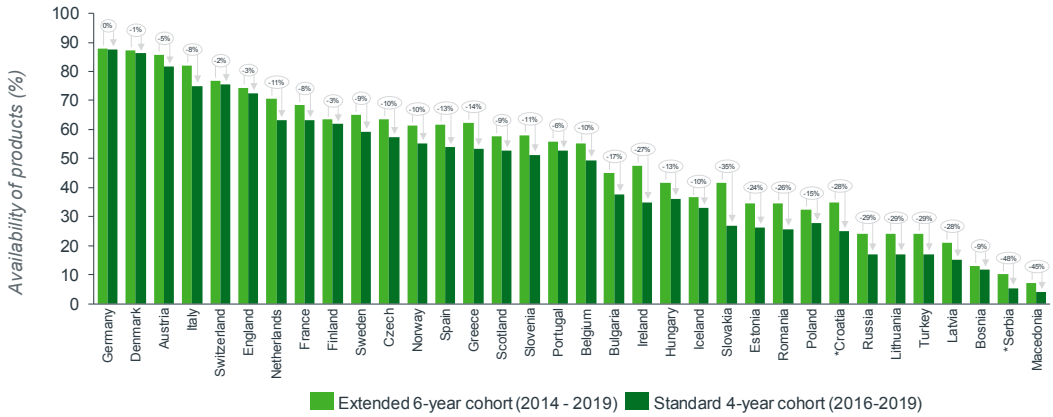
However, in many markets the P&R process does not start automatically; this requires a submission by the company or decision by those in the assessment process. This depends on the rules: the process in some countries is possible prior to marketing authorisation, but in others this requires a positive opinion from the EMA Committee for Medicinal Products for Human Use (CHMP), or even a formal decision from the EC or a

30 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.

31 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.

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.[32] 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.

Figure 9: A comparison of availability over a four and six year window



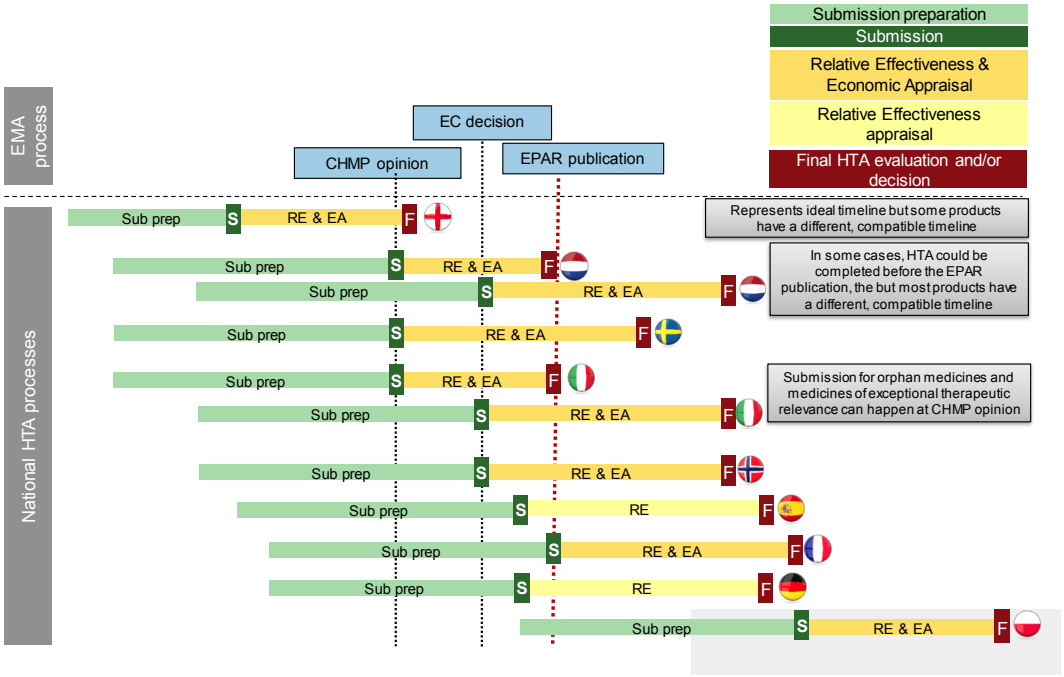
*Source: IQVIA - †In most countries availability equates to granting of access to the reimbursement list, except in DK, FI, NO, SE some hospital products are not covered by the general reimbursement scheme. *Countries with asterisks did not complete a full dataset and therefore availability may be unrepresentative.*

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.[33] The different times to submission are illustrated in the figure below.

32 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.

33 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 10: Time until initiation of the reimbursement process



Source: EFPIA; EPAR refers to European public assessment report

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.[34]

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.[35] For that

34 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

35 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

reason, companies are often inclined to not start an application until authorisation to enter the European market has been confirmed.

Figure 11: Percentage of products available in EU countries, segmented by company size

Ranked by total available medicines (EFPIA WAIT)

Country	*Top 20 Global Pharma (n=133 products)	SME and other biotech (n=105 products)
Germany	92%	83%
Denmark	98%	73%
Austria	94%	75%
Italy	90%	71%
France	76%	59%
Netherlands	88%	49%
Finland	80%	42%
Sweden	84%	41%
Czech	81%	41%
Spain	79%	40%
Greece	74%	47%
Portugal	76%	30%
Slovenia	78%	32%
Belgium	77%	27%
Bulgaria	65%	20%
Hungary	61%	17%
Ireland	65%	26%
Estonia	57%	15%
Poland	47%	14%
Slovakia	50%	30%
Romania	46%	20%
Croatia	55%	10%
Lithuania	38%	6%
Latvia	33%	6%

Source: The Patient W.A.I.T. Indicator 2020; Top 20 Global Pharma segmented by full year 2020 Rx sales

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.

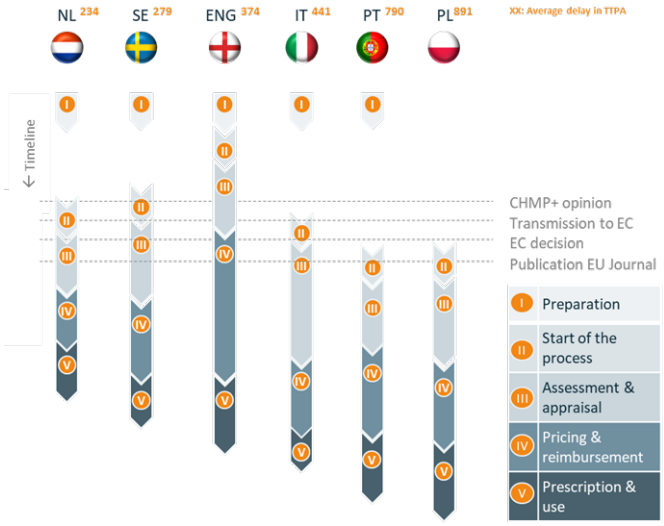
The length of time taken should reflect the EU Transparency Directive (European Commission, 1988). The purpose of this directive is to ensure the transparency of measures that regulate P&R of medicinal products. It sets a strict maximum time of 180 days for reaching a national P&R. This timeline starts 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 12: 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.[36]
- 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.[37]

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

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

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

be a 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.

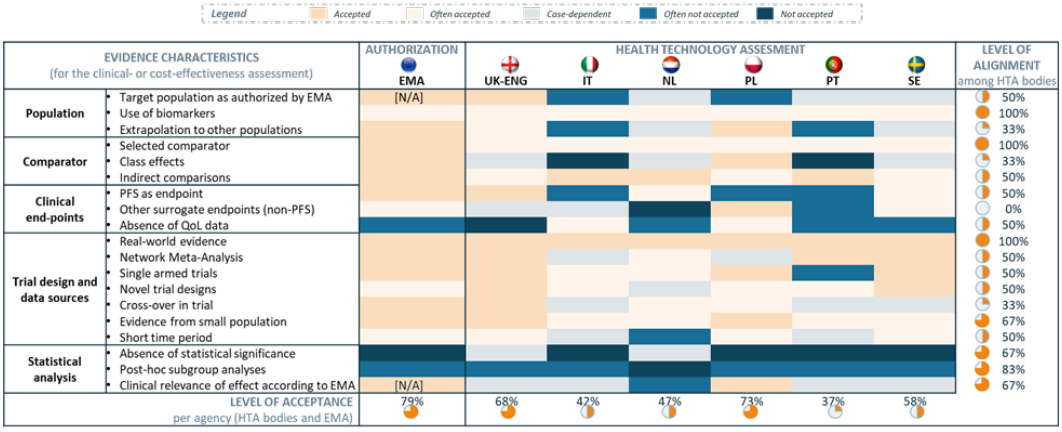
Misalignment on evidence requirement

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 13: 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

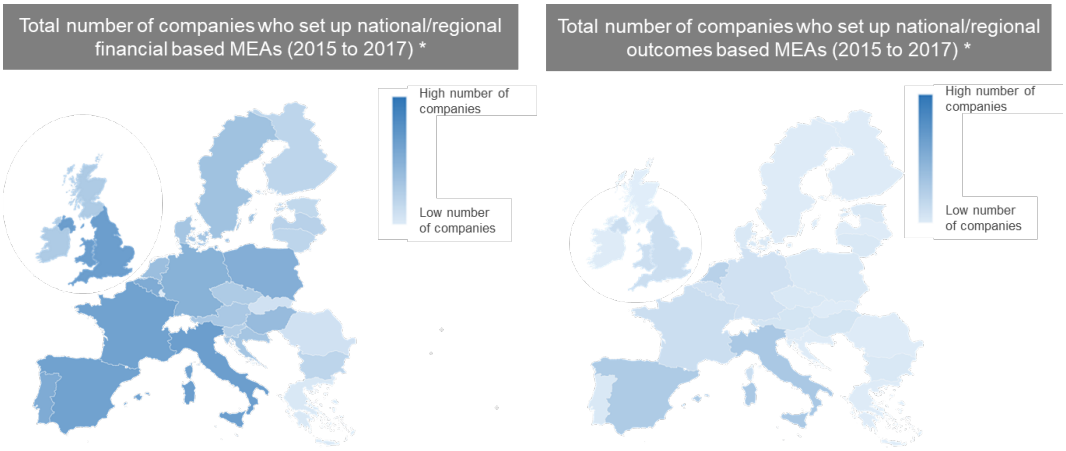
Next, even if there is agreement on the evidence regarding the value of a medicine, different countries have different levels of income and hence ability to pay. Decision makers are faced with the enormous challenge of striking a balance between fast patient

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.[38]

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 14: 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

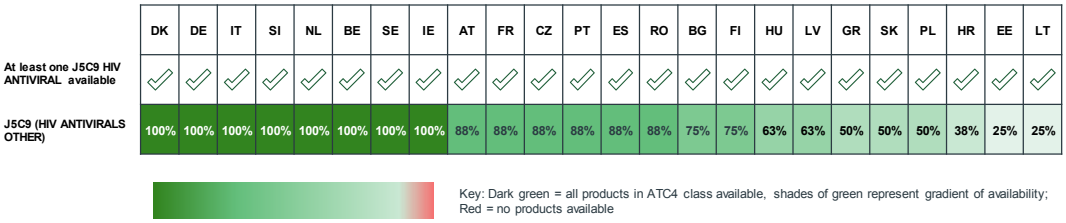
38 Time to Entry for New Cancer Medicines: From European Union–Wide Marketing Authorization to Patient Access in Belgium, Estonia, Scotland, and Sweden. Ferrario, A. Health Policy Analysis. *Value in Health* 21(7): 809–821, 01 July 2018

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.

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



Source: IQVIA analysis of The Patient W.A.I.T. Indicator 2020; n=8

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.

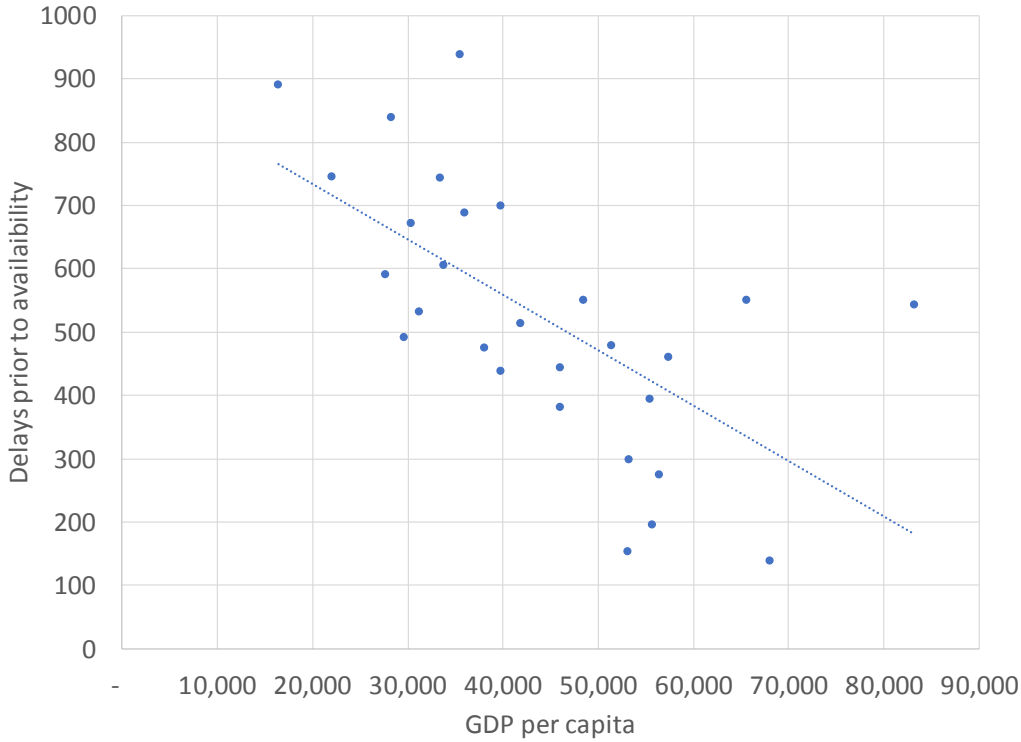
Insufficient budget to implement decisions

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 latest data from the OECD (2017) 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 16: 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.[39]

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 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

39 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

infrastructure and expertise (e.g. number of geneticists) available.[40] 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.[41] 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.[42]

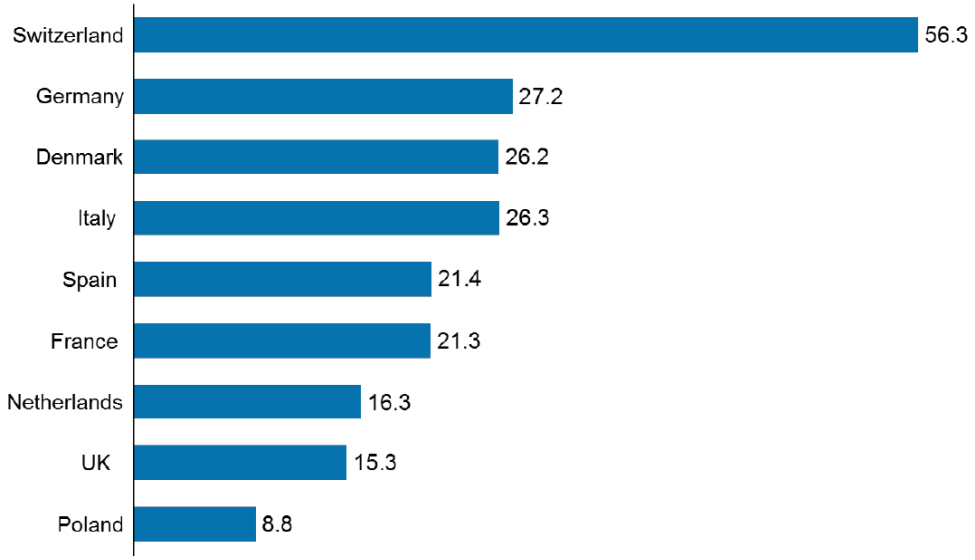
As a result – given that the number of patients for rare diseases may be very low, and finding these patients may be difficult – ensuring appropriate use and pharmacovigilance is challenging and the commercial viability of applying for reimbursement does not currently exist.

40 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

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

42 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

Figure 17: Investment in in vitro diagnostics (per capita expenditure on in vitro diagnostics (€) (2016))



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.[43]

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

43 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

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 are available to date (July 2016)) was 293 days.[44] Although the academic literature has focused on Italy, this applies to many markets in Europe.

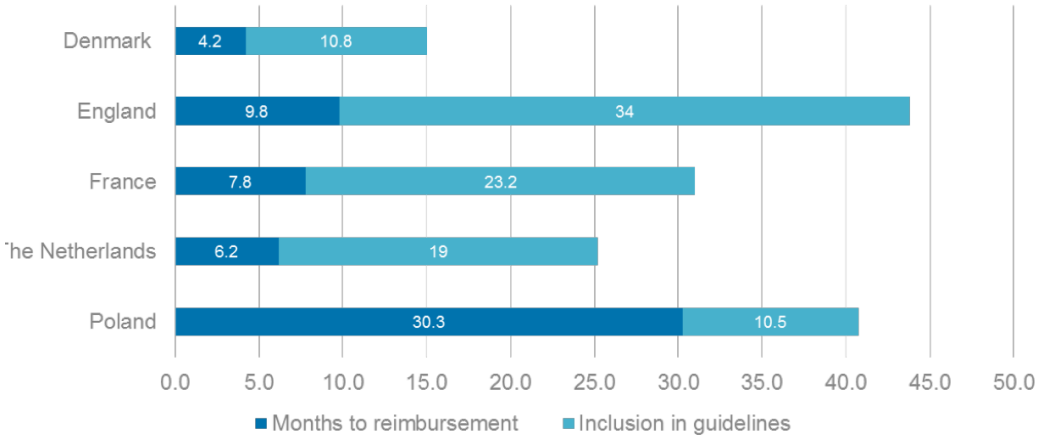
1.6. Availability is not access

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:

- 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 18: Average access timeline for personalised oncology medicines



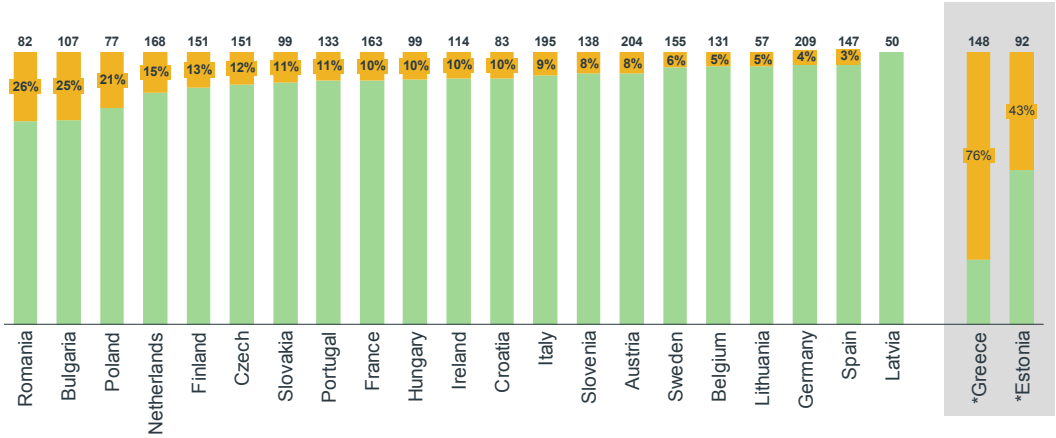
Source: EBE Personalised Medicine Report

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.

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

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



*Source: The Patient W.A.I.T. Indicator 2020; IQVIA MIDAS Q4 2020; Analysis includes 223 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. *Indicates countries where IQVIA data does 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:[45]

- 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

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

45 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/

patients across Europe have new medicines and therapies in their countries quickly".[46] 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 calls for a High-Level Multi-Stakeholder Forum on Access to Innovation.

This forum should be used as a vehicle to jointly create proposals that address the issues of unavailability and delay. Given the different root causes, there are five areas where proposals could be developed:

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. [47] 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

EFPIA already contributes to transparency on unavailability and delay with its yearly published 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.

There are a number of ways transparency could be improved. Horizon-scanning improves transparency regarding future products, facilitating early dialogue and consideration of health system consequences. This already occurs in some member states, but there is an opportunity for joint horizon-scanning.

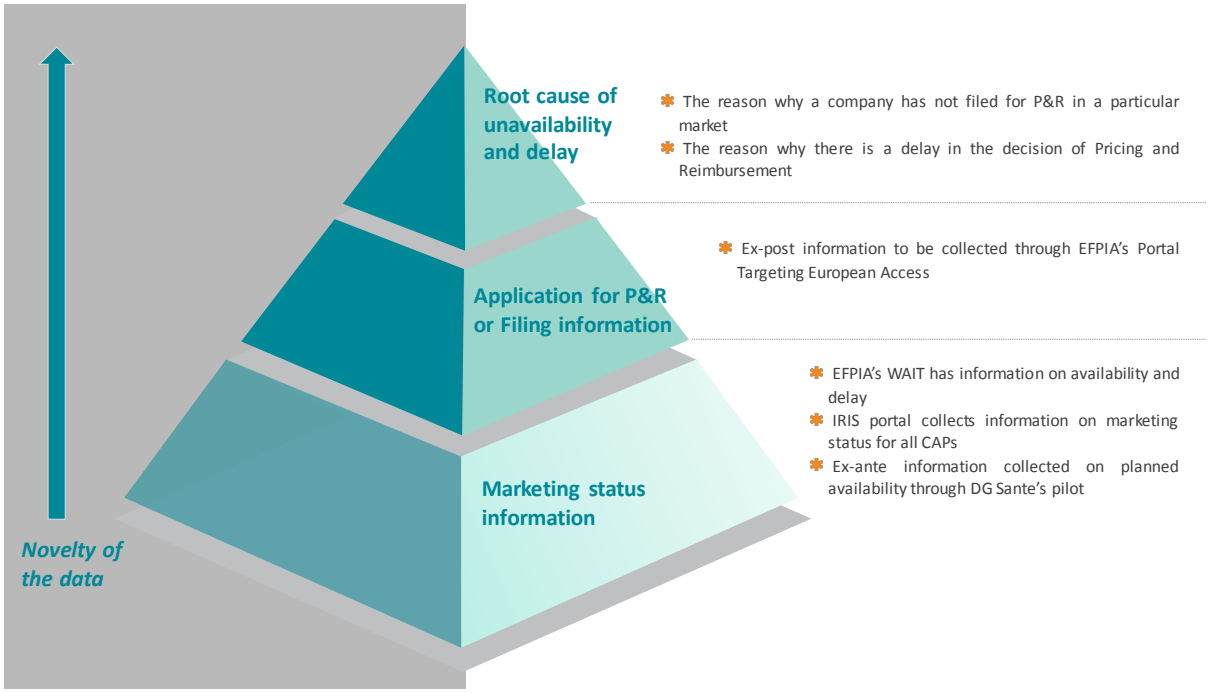
46 As set out in the European Commission's Pharmaceutical Strategy Roadmap - https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12421-Pharmaceutical-Strategy-Timely-patient-access-to-affordable-medicines

47 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

In order to further improve information regarding root causes of unavailability and delay the industry is investigating ways to monitor European Access hurdles. This could include timely collection of the considerations underlying unavailability and the degree to which this reflects (a) barriers within the environment, and (b) commercial decisions arising in light of the Member States' pricing and reimbursement processes. EFPIA proposes the collation of information from Marketing Authorisation Holders of centrally approved medicines regarding the timing and processing of pricing and reimbursement applications of their centrally approved medicines on a voluntary basis. This would include ex post information regarding products with a marketing authorisation during a fixed window of time. The proposed mechanism would be designed ensuring minimal burden for companies (it would be based on published regulatory data, data submitted to EMA IRIS Portal and the existing W.A.I.T. database) and to be in compliance with EU competition law.

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

Figure 20: Potential for more granular data on unavailability and delay



The proposal is currently being tested and discussed with interested stakeholders.

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

This includes encouraging the flexibility for Novel Payment and Pricing models. The industry believes that when used appropriately and tailored to the situation, novel pricing and payment models can accelerate patient access, allowing payers to manage clinical uncertainty, budget impact and sustainability of the healthcare system, whilst providing sufficient incentives for innovation. 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.

Proposals to improve the efficiency and quality of value assessment

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. EFPIA member companies remain committed to contributing to achieving an efficient system of European assessments of relative efficacy at time of launch.

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

New approaches that improve access need to be considered. Conceptually Equity-Based Tiered Pricing could improve access but it needs to be anchored in in the concept of solidarity — including a recognition that wealthier EU Member States should not benefit from the lower prices that ought to be available, in the interests of patient access, to less resourceful Member States. This cannot be solved on a country by country basis but would likely require an intergovernmental framework articulating solidarity/affordability for different EU countries and addressing specific issues related to the EU internal market and external reference pricing. Any discussion needs to take into account the broader global context and spill-over effects to other regions.

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.

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).