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EXPLORING THE FEASIBILITY OF MONITORING ACCESS TO NOVEL MEDICINES

A PILOT STUDY IN EU MEMBER STATES

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Exploring the feasibility of monitoring access to novel medicines: a pilot study in EU Member States

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Abstract

Ensuring affordable access to novel medicines has been identified as a policy priority among OECD and EU countries, yet systematic monitoring of the various dimensions of access is lacking. Previous efforts to measure access have focused primarily on one or at most two of these dimensions, such as availability and affordability, but a more holistic picture is needed. The OECD undertook a pilot study in EU Member States that aimed to determine the utility and feasibility of routine, cross-national monitoring of access to medicines across multiple dimensions. The work included a desk review to define the dimensions of access and associated indicators, followed by an OECD survey to explore the feasibility of collecting and analysing the relevant data for a convenience sample of 15 recently authorised product/indication pairs. This Working Paper presents key learnings from the desk review and country survey to which 21 EU Member States responded, with a focus on exploring the *utility* and *feasibility* of the processes of monitoring and measurement.

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This document presents supplementary material available online:
https://www.oecd.org/health/Suppl-Mat-monitoring-access-to-novel-medicines-EU-2023.pdf.

Country abbreviations

Austria	AUT
Belgium	BEL
Bulgaria	BGR
Czech Republic	CZE
Cyprus[1]	CYP
Estonia	EST
Finland	FIN
France	FRA
Germany	DEU
Greece	GRC
Hungary	HUN
Iceland	ISL
Italy	ITA
Lithuania	LTU
Luxembourg	LUX
Malta	MLT
Norway	NOR
Portugal	POR
Slovenia	SVN
Spain	ESP
Sweden	SWE

[1] Note by Türkiye: The information in this document with reference to “Cyprus” relates to the southern part of the Island. There is no single authority representing both Turkish and Greek Cypriot people on the Island. Türkiye recognises the Turkish Republic of Northern Cyprus (TRNC). Until a lasting and equitable solution is found within the context of the United Nations, Türkiye shall preserve its position concerning the “Cyprus issue”.

Note by all the European Union Member States of the OECD and the European Union: The Republic of Cyprus is recognised by all members of the United Nations with the exception of Türkiye. The information in this document relates to the area under the effective control of the Government of the Republic of Cyprus.

Executive Summary

Access to medicines is a critical issue for both patients and health systems, but it is known to vary considerably both across the OECD, and within the EU. While ensuring affordable access to novel medicines has been identified as a priority among OECD and EU countries, **systematic monitoring is lacking**. For medicines, access encompasses the multiple dimensions of availability, affordability, accessibility, acceptability, and quality. Each of these dimensions involves multiple elements that relate to events in the lifecycle of a medicine – namely marketing authorisation, health technology assessment, coverage and pricing determinations, timing of product launch, clinical guidelines, prescribing and dispensing, and finally patient utilisation. Previous efforts to measure access, however, have generally focused primarily on availability and affordability, with availability often presented as simple proportions of the number of medicines covered (or reimbursed) in full or in part by third-party payers.

This paper presents some key learnings from a pilot study in EU Member States that aimed to determine the *utility* and *feasibility* of cross-national monitoring of access to novel medicines across multiple dimensions. Using a convenience sample of 15 novel medicine and treatment indication pairs (i.e. products/indications) representing different medicine archetypes and therapeutic areas, retrospective data from 21 countries were collected via an OECD survey covering different aspects of access relative to the lifecycle of each sample medicine. Several indicators were generated reflecting the dimensions of **availability, affordability, accessibility**, and **acceptability**. Table 1 below summarises the key findings and highlights some of the challenges in the data collection, analysis, and interpretation of those indicators. Given the small but highly heterogenous sample of medicines, and significant challenges in data availability, these results cannot be interpreted as a holistic reflection of the landscape of access across countries. Nevertheless, they are useful in illustrating the types of analyses that can be undertaken – and their limitations – and providing useful insights that could inform future analyses.

The findings of this study highlight the value of using a broader set of indicators and looking at access across multiple dimensions. While it was possible to generate indicators for most countries that went beyond existing measures and attempted to account for other contextual factors, the presented indicators can be misleading – largely due to the presence of confounders, lack of data transparency, and the challenges in adequately accounting for contextual complexities. For example, time-to-access estimates may suggest avoidable delays in national processes ameliorable to policy intervention, or may simply reflect differences in industry launch sequences, beyond the control of policy makers. Confidentiality of pricing and reimbursement data confounds measurement of affordability to health systems, as estimates are distorted by the potential but undisclosed existence of discounts and rebates. Individual health system features, such as early access coverage schemes and complex cost-sharing mechanisms are challenging to account for in routine measures of access, but their exclusion can lead to misinterpretation and misrepresentation of the current landscape of access. Finally, measures of individual medicine availability that do not take into account availability of appropriate therapeutic alternatives raise a seminal question regarding the value of assessing access to individual medicines *vis a vis* measuring access to *treatment*.

Overall, attempting to measure access at the product/indication-level across multiple dimensions proved to be a highly complex exercise. While responding countries were generally able to provide nationally representative data, the feasibility of collecting detailed information was hampered by the heterogeneity of data sources used by the responding country institutions. In most cases, the requested survey data were only partially publicly available, and some respondents drew on additional (at times, confidential) internal data sources. Much of the data requested were not collected routinely and, in some countries, legal provisions precluded the publication of data for individual medicines.

Further development or expansion of this work beyond this pilot study would benefit from the following, while also recognising that there will be an inherent trade-off between accuracy, comprehensiveness and feasibility of any indicators produced moving forward:

- **Greater clarity around the objectives of monitoring and measurement of access**, and consideration of whether other approaches may be more appropriate. Most countries that responded to the survey do not systematically measure or monitor access to medicines on a national level; of those that do, some focus on the efficiency of processes, others on measures of overall consumption or expenditure. A **multistakeholder consultation** could be used to develop consensus around what should be measured routinely to inform policymakers, including whether measuring access to *treatment* as distinct from access to individual medicines may be more appropriate.
- **Agreement on the indicators that should be prioritised**. Some indicators are more suitable for routine collection than others, such as those with data in the public domain or in existing sharing platforms. Going forward, it will be important to develop some consensus on the indicators of highest priority, utilising criteria such as such as policy-relevance, accessibility, comparability etc.
- **Agreement on the scope of analysis for periodic assessment.** Analyses may need to distinguish between outpatient and inpatient products, or consider them separately, given the differences in country processes and data availability. Some indicators may be more appropriate for measuring access to a medicine archetype or therapeutic class, rather than an individual medicine. For example, an analysis of access to breakthrough therapies used in the treatment of rare diseases could be appropriate, given that these products may be subject to exceptional evaluation processes.
- **Development of agreed methods for collecting, exchanging, and interpreting data,** with consideration of individual country contexts. Taking into account the structure of the health care system, and the regulation, selection, coverage and pricing policies in place, can help in framing and interpreting the results. While it may not be possible to control for these factors, cross-country comparisons could be facilitated by grouping countries with common health system characteristics that could affect specific indicators.
- **Investment in improving the evidence base,** which involves the willingness of countries to systematically collect and share the necessary data. The lack of transparency in the area of pharmaceutical coverage, pricing, and utilisation not only hinders the routine analysis of data, but also the generation of reliable evidence to inform important policy questions. Where possible, priority indicators should draw on existing data sources, but where these are unavailable, they should be a priority for development.

Table 1. Key insights from this pilot study

Indicator	Key findings	Key considerations for:	
		Utility	Feasibility
Availability			
Proportion of medicines covered (in full or in part by public budgets/third party payment)	14 of 21 countries reported coverage of ≥ 80% of the sample, however: — 17 of 21 countries when alternatives taken into account — most countries reported limitations in coverage relative to the authorised indication	Simple counts of covered medicines do not capture: — availability of therapeutic alternatives — progress within the coverage process for medicines not yet covered — impact of limitations on coverage — existence of alternative access mechanisms	Broadening data collection beyond coverage status introduces additional challenges in that data: — may be held by different institutions and/or not publicly available — are unlikely to be in standardised format — may not be available for inpatient products
Time-to-access, e.g. median time to positive coverage decision from date of marketing authorisation (early access coverage excluded) — with decomposition	Time from MA to coverage ranged from 1 – 2 years for most countries, however: — time-to-first HTA and/or coverage application varied (3 –12 months) — time from first coverage application to positive decision accounted for the longest delays —first sales often within one month of a positive decision	Linear measures such as the time between MA and positive coverage decision do not account for: — company launch sequences — differences in the nature and timing of national coverage processes —product-dependent effects, including multiple submission attempts and clock stops — existence of early access coverage schemes	Broadening data collection to decompose measurements into different time periods introduces additional challenges: — lack of publicly available data — data held by multiple institutions — data not collected nor tracked routinely
Affordability			
System affordability: Annual treatment cost based on ex-factory prices, relative to GDP per capita	Relative affordability for a given product varied significantly, however: —confidential rebates and discounts existed in more than 70% of country-product/indication pairs	Affordability estimates of individual medicines are confounded by: — lack of transparency of net prices — inability to consider cross country variations in levels of consumption (or number of eligible patients) and expenditure	While official pricing data are often at least partially publicly accessible: — inpatient data are less readily accessible — existence of rebates & discounts is considered commercially confidential
Patient affordability: Monthly out-of-pocket cost, relative to average daily wage	Financial burden for a given product varied significantly, with the highest financial burden where patient contributions were structured as coinsurance	Affordability estimates of individual medicines are confounded by the complexity of cost-sharing mechanisms, which may vary with the setting of administration and patient characteristics	Data on out-of-pocket costs are sparse
Accessibility			
Total volume sold (or number of patients treated) in a fixed time period relative to total population size	Large differences in consumption and patient numbers were seen across countries for each sample medicine	Accessibility estimates based on individual medicines are confounded by: — prevalence of disease — differences in clinical practice (including availability of alternatives) — approval in multiple indications — setting of administration	Utilisation data generally not publicly available, though some countries share data on collaborative platforms (albeit with reporting delays). Data: — cannot be disaggregated by indication — are considered commercially sensitive in some countries — are less readily available for inpatient sector — may not be collected routinely
Acceptability			
Proportion of covered medicines with consistency between covered indication and clinical guidelines	Coverage was consistent with the clinical guidelines in almost all cases	Simple counts do not account for cross country variations in clinical guidelines/ practice	Assessment is challenging and not attempted routinely: — data are not readily available (multiple sources) — delays in update of clinical guidelines are frequent

Note: MA marketing authorisation. HTA health technology assessment.
Source: OECD survey on access to novel medicines 2021.

1. Efforts to measure access do not always reflect its multidimensional nature

1. Affordable access to medicines is essential to achieving effective universal health coverage, with UN *Sustainable Development Goal* number 3.8 emphasising the importance of "access to safe, effective, quality and affordable essential medicines and vaccines for all" (United Nations, 2017[1]). Yet although access to medicines is a critical issue for both patients and health systems, it is known to vary considerably across both the OECD, and within the EU. In health care, access can be broadly defined as "*the ability to obtain health care services based on medical need and irrespective of factors that are not related to need, such as physical location, socio-economic status, or income and ability to pay*" (Oliver and Mossialos, 2004[2]). With respect to medicines, this includes whether medicines hold marketing authorisation (i.e. have regulatory approval), whether they are affordable to individuals and the health system, and whether they are available and physically accessible. Factors that can adversely affect access include high prices and large out of pocket costs; launch strategies by companies; delay in or denial of coverage or reimbursement; and importantly, individual health system characteristics.

2. Thus far, initiatives to assess and compare access to medicines across countries have generally been led by academic institutions, patient associations, or the pharmaceutical industry, and have often been opportunistic, drawing on incomplete information and at times, giving rise to conflicting information[2]. Several have relied on marketing authorisation (as a proxy for availability), coverage status of medicines (as a proxy for affordability), and/or sales data (as a proxy for accessibility). While studies sponsored by the industry have focused on access to newly-approved treatments (e.g. (Vintura, 2020[3]; EFPIA, 2022[4]; EFPIA, 2021[5]), others have focused on selected categories of medicines (e.g. orphan medicines, oncology medicines, medicines for rheumatoid and cardiovascular conditions, essential medicines – (Zhang, Chantel Hueser and Hernandez, 2017[6]; Cherny et al., 2016[7]; Cherny et al., 2017[8]; Zamora et al., 2019[9]; Wirtz et al., 2016[10]; Putrik et al., 2014[11]; World Health Organization, 2018[12]; Hofmarcher et al., 2019[13]; Chapman, Paris and Lopert, 2020[14]).

3. Ensuring access to affordable, novel medicines has been identified as a priority among OECD and EU countries, yet systematic monitoring of the situation is lacking. One of the four pillars of the 2020 EU Pharmaceutical Strategy[3] aims to ensure affordable access to medicines for patients, and to address unmet medical needs in the areas of cancer, rare diseases, and antimicrobial resistance. In line with this, the *European Medicines Agencies Network Strategy to 2025* on availability and accessibility of medicines proposes increasing transparency, including on the marketing status of centrally authorised medicines in EU Member States[4]. The network strategy also proposes developing better metrics as a basis for cross-

[2] For a more detailed discussion, see the OECD Health Working Paper No. 123 by Chapman, Paris and Lopert (2020[14]) on the topic of *Challenges in access to oncology medicines: Policies and practices across the OECD and the EU.*

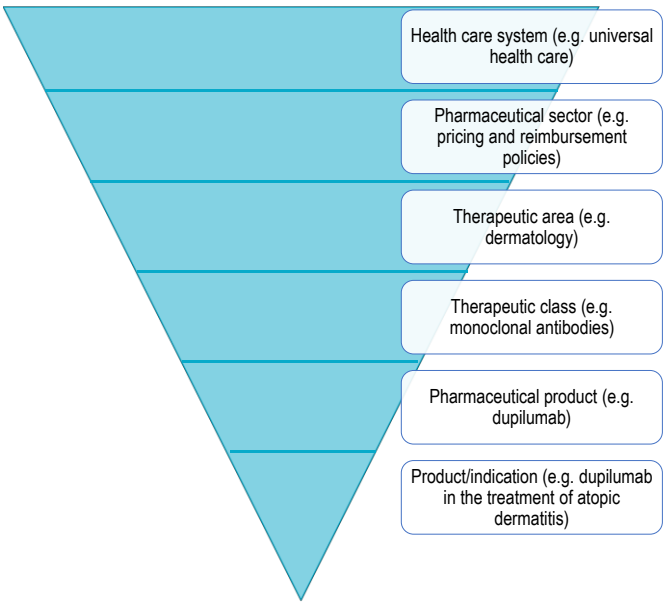
[3] See https://ec.europa.eu/health/human-use/strategy_en, accessed May 2021.

[4] See https://www.ema.europa.eu/en/documents/report/european-union-medicines-agencies-network-strategy-2025-protecting-public-health-time-rapid-change_en.pdf, accessed May 2021.

country comparisons of accessibility by patients, including the impact of programs to provide early access prior to a national coverage decision (ibid.). Furthermore, the *Lancet Commission on Essential Medicines Polices 2017* recommended that governments and health systems "create and maintain information systems for the routine monitoring of data on the affordability, price, and availability of essential medicines, in the public and private sectors" (Wirtz et al., 2017[15]).

4. Conceptually, indicators used to measure or monitor access to medicines can be developed at different levels, depending on the desired research or policy questions (Figure 1.1). Health care or pharmaceutical system-level indicators are useful if the intention is to describe, measure, and analyse systems and policies across countries. For example, these types of indicators include contextual factors such as the way countries organise and finance their health systems and evaluate and reimburse medicines (Section 1.3). Metrics can also be assessed for groups of products in aggregate, for example collected and presented at the level of the therapeutic area (e.g. dermatology) or even therapeutic class (e.g. monoclonal antibodies). These types of metrics provide insight into access to treatment for specific patient populations. However, if the intention is to compare overall access to all (or a subset) of newly authorised medicines, often of primary interest to policy makers, then granular data can be collected at the level of the active substance, or the active substance in one or more of its approved indications. Generated indicators may then be presented in aggregate across the sample (and interpreted as such if data are representative) or for individual products and/or products/indications. Collecting and interpreting results at any level requires an understanding of the potential caveats and confounders, as well as limitations in the available data.

Figure 1.1. Access indicators can be developed at different levels



Note: Here, "pharmaceutical product" also refers to the active substance or molecule e.g. dupilumab.
Source: Authors.

5. Given OECD member countries' expressed interest in ensuring affordable access to novel medicines, this paper presents findings of an OECD pilot study on assessing the feasibility of monitoring this, using data collected at the product/indication-level. The aim of this project was to determine the *utility* and *feasibility* of systematic and periodic cross-national monitoring of access to novel medicines across multiple dimensions, and if feasible, to propose an approach for regular and repeated reporting. The underlying objective was to facilitate cross-country comparisons of access using standardised indicators applied to selected product/indication pairs (i.e. at the lowest level in Figure 1.1), while recognising that

access should be considered within the context and characteristics of each country's health care system. Given the complexity of this exercise, and as a concession to pragmatism, the work was undertaken as a pilot study among EU Member States, which have a centralised process for the granting of marketing authorisation of medicines.

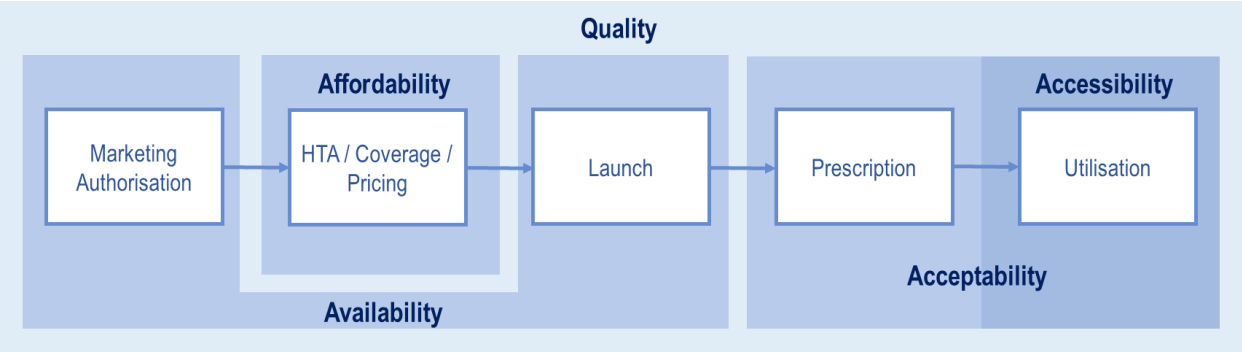
6. The paper is organised as follows:

- Section 1. presents the results from a rapid review of published and grey literature to define the multiple dimensions of access and associated indicators, to be applied as an analytical framework for the selection of indicators of access. This section also introduces the OECD survey, followed by a discussion on the contextual considerations in interpreting access measures.
- Sections 2. to 5. present the key learnings from the OECD survey to which 21 EU Member States responded, organised by the access dimensions explored: **availability, affordability, accessibility**, and **acceptability**. Here, the focus was on exploring the utility and feasibility of monitoring and measurement, rather than on results.
- Section 6. outlines some of the main lessons learned from this study as well as considerations for next steps.
- Annexes A to G in the online Supplementary Material provide additional information, as referenced throughout the paper. Annex A also contains a glossary of some of the main terms used.

1.1. Access is a multidimensional concept influenced by many factors

7. "Access" to medicines may be viewed as encompassing five dimensions: availability, affordability, accessibility (geographical), acceptability (rational selection and appropriate use), and a cross-cutting dimension of quality, each described briefly below (Management Sciences for Health, 2012[16]; Bigdeli et al., 2013[17]; Chapman, Paris and Lopert, 2020[14]; World Health Organization, 2004[18]). Each of these dimensions involves multiple elements and relates to specific events in the lifecycle of new medicines – namely marketing authorisation, health technology assessment (HTA), coverage and pricing determinations; timing of product launch[5]; clinical guidelines, prescribing and dispensing; and finally patient utilisation (see Figure 1.2). It should be noted that the dimensions cannot be considered mutually exclusive.

Figure 1.2. Dimensions of access relative to the lifecycle of a medicine



Note: HTA health technology assessment. Dimensions of access cannot be considered mutually exclusive.
Source: Authors.

[5] *Launch* has a variety of definitions. According to EU legislation, launch refers to the *actual placing of the medicinal product on the Union market* i.e that one presentation of the product has been released (first made available) into the distribution chain in at least one Member State (Directive 2001/83/EC; Art. 14 of Regulation 726/2004; Notice to Applicants Volume 2A, Chapter 1 Section 2.4.2). Other definitions of launch include when the product first appears in a national pharmacy / prescribing database, or the first sale in the national context.

8. The Secretariat applied this as a framework for attempting to define a set of indicators that could capture the multiple dimensions of access, and thereby develop, as far as possible, a more robust basis for cross-country comparisons of individual product/indication pairs. Prior efforts to measure access to medicines have focused primarily on the dimensions of availability and/or affordability of a subset of products at a defined moment in time, published at an aggregate level (see some examples of existing initiatives in Annex B). Some examples of indicators that could be, or have previously been, reported reflecting the different dimensions at the individual product/indication-level are discussed below, with further details on their description, purpose, necessary data elements and sources of data described in Annex C. Box 1.1 details a non-exhaustive list of some of these potential indicators per access dimension. However, it is also important to consider the utility and feasibility of collecting and interpreting product/indication-level indicators from countries. This depends in part on the structure of the health care system and the regulation, selection, coverage, and pricing policies in place. Consequently, indicators of access need to be viewed against a backdrop of the characteristics of each country's health care system (see Section 1.3).

Box 1.1. Access indicators can be explored by dimension

Potential indicators that could be explored using a defined *sample* of product/indication pairs are described below. Note that the fifth dimension of *quality* was not considered in this paper for feasibility reasons.

Availability

- Proportion of medicines (or appropriate alternative) covered
- Proportion of medicines covered, including the extent of coverage relative to its marketing authorisation
- Proportion of medicines covered, including any additional limitations or restrictions on coverage
- Average (or median) time to application for health technology assessment and/or coverage from marketing authorisation (e.g. 6 months, +12 months, +2 years)
- Average (or median) time to coverage from marketing authorisation (e.g. 6 months, +12 months, +2 years)

Affordability

- Average (monthly or annual) treatment cost, relative to per capita GDP
- Average (monthly or annual) out-of-pocket treatment cost, relative to wage

Accessibility

- Number of patients or total volume sold in a fixed time period relative to total population size
- Average time to first (covered) sales from marketing authorisation

Acceptability

- Proportion of covered medicines with consistency between covered indication and clinical guidelines
- Proportion of covered medicines with added therapeutic value over alternatives

Source: Authors, based on desk review and prior knowledge and research.

1.1.1. Availability

9. Availability in a general sense refers to the relationship between the amount of product or service needed and the amount able to be provided (Management Sciences for Health, 2012[16]; Wirtz et al., 2016[10]; Bigdeli et al., 2013[17]). From the literature, this can be based on availability via early access or compassionate use schemes, existence of marketing authorisation, being offered for sale by marketing authorisation holders (MAH), covered by health insurance scheme(s), on pharmacy shelves ready to be dispensed, or sales volumes over a given period of time. The dimension of availability can also be perceived more narrowly, including information about events such as the occurrence of shortages, which

may lead to medicines not being available for a limited period of time. It is also sometimes difficult to distinguish availability from the dimension of accessibility.

10. The concept of availability considered in this project relates predominantly to the first essential condition for ensuring access to medicines: availability in the country market. For novel medicines in the EU, this is predicated on the granting of a (centralised EU) marketing authorisation for a product in one or multiple indications, followed by launch of the medicine by the MAH (in a specific country). While manufacturers in the EU are authorised to launch their products as soon as marketing authorisation is granted, in some countries they may choose to wait for a decision on coverage and pricing by one or more third-party payers, for example where sales are likely to be limited in the absence of third party payment, or in the case of small markets or the presence of external reference pricing (Kanavos et al., 2010[19]; Danzon and Epstein, 2012[20]). Early access schemes (EAS) are also considered as a separate, but related, issue to availability, as these schemes often focus on very small patient populations or patient numbers with specific restrictions on use and cannot be considered as general access mechanisms (see Box 1.2). Nevertheless, some countries fund EAS targeting wider populations as further described in Box 1.2 and Box 2.1.

11. With regard to availability, and timeliness of availability of a medicine for a given indication in a given country, relevant indicators include (see Annex C, for further details):

- Existence of a valid marketing authorisation for the particular indication (as a prerequisite);
- Whether or not an application for coverage / pricing[6] has been made;
- Whether or not a medicine is covered by public budgets;
- Whether or not a medicine has been sold (e.g. as a proxy for launch status); and
- Time-to-access indicators, such as differences between marketing authorisation and different country processes (e.g. marketing authorisation to launch - see Table AC.2, Annex C, for other examples).

12. It is important to recognise the limitation that *availability* of specific product/indication pairs does not reflect *availability* or *access* to treatment if there are other appropriate alternatives available, nor does it consider the issue of medicine shortages.

[6] In some countries with a health technology assessment (HTA) process, an HTA dossier will be submitted prior to or simultaneously with an application for coverage and pricing.

Box 1.2. Early access schemes are considered as a separate, but related, aspect of availability

Early access schemes (EAS) as defined in this paper predominantly relate to a scheme or program that makes a product available to a limited number of patients at the initial stages in the lifecycle of a medicine i.e. *prior* to a marketing authorisation and/or the publicly funded coverage decision in a country. These schemes generally apply to promising therapies used in severe diseases with high unmet need and no therapeutic alternatives.

There are different types of EAS, such as those that provide access to individual patients (*named-patient programs*) or compassionate use programs initiated by pharmaceutical companies for a group of patients in a selected clinic or hospital (*population-based programs*). In some countries, population-based programs are broader and extend to the entire target population within the scope of an authorised indication. Early access schemes also vary in relation to their funding arrangements, and are either funded by pharmaceutical companies (i.e. *industry-sponsored*) or third-party payers (i.e. *government or insurer sponsored*). Given that the majority of EAS focus on very small patient populations or patient numbers with specific restrictions on use, they cannot be considered as general access mechanisms. However, it is recognised that some countries have publicly funded schemes targeting wider patient populations; this paper refers to publicly funded population-based programmes that benefit the entire target population within an indication as "*early access coverage schemes*" (see the example for France in Box 2.1, as well as other examples of different schemes).

Early access schemes vary significantly across countries, and they may impact measurements of time-to-access. Where third-party payers fund access under these programmes, companies may feel less pressure to gain agreement on price. Though some reviews have already been published on existing EAS (e.g. (Balasubramanian et al., 2016[21])), it may be worthwhile examining the interactions between EAS and time-to-access. Potential indicators include the existence of an EAS; the type (population-based versus named-patient programme); funding arrangements (including pricing and reimbursement status and any patient contributions); the scope and conditions (i.e. restrictions and requirements e.g. maximum number patients included); duration (including collection of start and end dates); number of patients ultimately accessing the product through the scheme; and alignment with the eventual coverage decision.

Source: Authors as cited.

1.1.2. Affordability

13. Affordability can be considered as the relationship between price and ability to pay for a medicine, both at the individual level, for patients, and at the level of health systems and public budgets. For the vast majority of medicines entering the market for the first time, prices will well exceed the ability of any individual to pay out of pocket, and third-party funding is essential for individual affordability. In most OECD and EU countries, prescription medicines are covered in whole or in part by government or social health insurance programmes, albeit with different cost-sharing schemes, including co-payments, coinsurance, deductibles, extra billing, safety nets or caps (Paris et al., 2016[22]). Some payers automatically cover medicines once they receive marketing authorisation, while others first undertake a comprehensive review process, including health technology assessment, to assess costs and benefits and may choose to cover only those medicines found to be acceptably cost effective. Depending on the type and price of the medicine, affordability for patients may depend on: 1) whether the medicine is *covered* and if conditions of coverage restrict access relative to the terms of the marketing authorisation; and 2) whether user co-payments, where they exist, are excessive. Affordability for public budgets may depend on priority setting by governments and resource allocation and willingness-to-pay, not only limited to the health care sector.

14. Affordability to a medicine in a given country can be explored using the following indicators (see Annex C, for further details):

- Whether a medicine is covered or subsidised by public budgets more broadly, including the scope of coverage relative to its approved indication(s) for marketing, and any additional limitations or restrictions on coverage;
- Type and level of cost-sharing for individual products, including information on
  - coinsurance (fixed percentage of medical costs)
  - co-payment (fixed amount of payment for medical costs)
  - deductible (threshold for total costs above which insurance coverage begins)
  - extra-billing (difference between the price charged and reference price for reimbursement)
  - safety nets and caps;
- Average treatment price or cost relative to population wealth (at the system-level); and
- Average treatment price or cost relative to wage (at the patient-level)

1.1.3. Accessibility

15. Accessibility refers to the ability of a patient to obtain a prescription when it is needed. In some cases, this may refer only to physical accessibility for the patient i.e. geographical closeness to a prescriber or pharmacy, or ability to obtain an appointment. More broadly, it is also influenced by other elements in the pathway to the patient, such as the marketing authorisation, coverage and pricing decisions, inclusion in clinical guidelines and treatment protocols, doctors' willingness to prescribe, and pharmacists' willingness and ability to dispense. With increasing medicine shortages in OECD countries (Chapman, Dedet and Lopert, 2022[23]), the dimension of accessibility is increasingly important. Utilisation by patients for whom the medicine would be of benefit is arguably an indirect metric for accessibility but is challenging to measure. Indicators include, for example, utilisation measured using standard metrics such as defined daily dose (DDD)[7]/1000 population/day (see Annex C, for further details).

1.1.4. Acceptability

16. Acceptability relates to the attitudes and expectations of a product or service and its actual characteristics. With respect to medicines, this generally relates to rational use and appropriate prescribing, as well as patient adherence. Prescribers are a key influence on the dimension of acceptability. It is likely that for a medicine to be acceptable, it is included in clinical guidelines and/or treatment protocols, though in some cases acceptability will be influenced by industry promotion and detailing. The relationship between the clinical guideline and the level of reimbursement for a specific indication is relevant here. Perceived added therapeutic "value", could also influence acceptability. Broad access to all medicines is often assumed to be ideal, but may not in fact be essential – access to some medicines that are highly effective or cost-effective in comparison to standard care may provide greater benefit to patients and health systems than less effective ones. The presence of appropriate alternatives may contribute to this dimension (as well as to availability and accessibility). Consequently, indicators to measure acceptability include (see Annex C, for further details):

- Indication(s) for use included in (national or transnational) clinical guidelines or treatment protocols relative to those specified in the relevant coverage decision;
- Some measure of added therapeutic "value"; and
- Some measure of the availability of appropriate alternatives, whether within class or within indication.

[7] For products without a DDD, milligrams/1000/day or international units/1000/day could be computed.

1.1.5. Quality

17. The quality of medicines is sometimes described in the literature as a crosscutting dimension of access (Management Sciences for Health, 2012[16]). Quality issues may arise at the level of the manufacturing facility, specific production process in a given facility, or be due to logistical or transportation problems. Similarly, the safety of all medicines, including adverse effects or other medicine-related problems, is monitored through pharmacovigilance systems. While quality and safety issues can affect access, this dimension was out of scope in this particular study.

1.2. The OECD surveyed EU Member States to explore the feasibility of generating access indicators across multiple dimensions

18. The remainder of this paper draws extensively on **lessons learned from a pilot survey of EU Member States distributed in November 2021**, to which a total of 21 countries responded as of May 2022 (Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Italy, Lithuania, Luxembourg, Malta, Norway, Portugal, Slovenia, Spain, and Sweden) (see Annex D, for more details). The survey aimed to gather information on various dimensions of access to a sample set of 15 novel medicines, valid as at 01 October 2021, in order to retrospectively compute and compile selected indicators of access. As 21 countries each responded to questions for a sample set of 15 product/indication pairs, the total sample dataset included 315 unique country-product/indication combinations.

19. **The results presented reflect those of a small convenience sample of heterogenous products and should not be considered representative of the access situation in each country.** Instead, they are intended to demonstrate the types of analyses that can be undertaken with these data and the limitations posed.

1.2.1. The OECD access survey drew on a convenience sample of 15 recently authorised product/indication pairs

20. A convenience sample of fifteen *index* product/indication pairs was chosen from among new active substances centrally authorised in the EU between 2015 to 2018 (allowing 3 years from the latest marketing authorisation of an active substance to 01 October 2021) – see (Table AD.1, Annex D). As this was a feasibility study, several factors were considered in selecting the index pairs. These included therapeutic class; monotherapy; number of indications; route of administration; care setting; availability of alternatives; uniqueness of indication; orphan status; nature of marketing authorisation etc. Efforts were made to:

- reflect a broad representation of the distribution of new active substances across therapeutic areas within the proposed timeframe;
- include a range of product archetypes (e.g. orphan drugs, approval under exceptional circumstances, accelerated approvals, and one advanced therapy medicinal product [ATMP]);
- prioritise products with a single main indication, as utilisation data are unlikely to be available disaggregated by indication;
- favour products administered predominantly in an ambulatory care setting (i.e. via oral or subcutaneous injections), as data may be more readily available; and
- select products without mandatory co-administration of another product, so “access” would not depend on the availability of another product.

1.2.2. Data covered seven domains, reported as at 01 October 2021

21. The data present a cross-sectional snapshot of various dimensions of access for the sample set of novel medicines as at 01 October 2021[8]. The survey covered seven broad topic areas, A to F: (A) early access schemes, (B) health technology assessment (HTA), (C) coverage and pricing, (D) treatment costs, (E) prescription, and (F) utilisation. Table AD.2 (Annex D) gives a high-level overview of the (conditional) questions asked for each index product/indication pair. Country Experts were requested to answer the questions with information valid as at 01 October 2021, and to the extent possible, ensure that responses reflected the specific indication specified in the initial marketing authorisation of the product in the European Union (see Table AD.3, Annex D, for an overview of responses by topic area). Subsequent indications were not considered. Experts were also asked to answer several questions on the sources and methods of data collection, to inform country comparisons and explore the feasibility of any future work (Table AD.4 and AD.5, Annex D). Country Experts included, for example, representatives from national insurance agencies, ministries of health, competent authorities for pricing and reimbursement, and HTA agencies.

22. Unless otherwise stated, the information presented reflects the national level situation for each product/indication pair. This is the case in all countries in which coverage decisions are made at the national level, applying to the whole country, and independent of setting of administration. In other countries, the information collected does not necessarily apply to all patients, care settings or regions. It is recognised that in some countries, coverage may vary between settings of care, but this was not considered as countries were permitted to provide only one response for each product/indication pair.

23. Given the complexity of this exercise and significant challenges in data availability, it was **not possible to compute all the anticipated indicators nor explore complex relationships between them.**

1.2.3. EURIPID data were used for validation and as an alternative data source in some cases

24. Medicine price data for 26 EU countries is already collected and maintained in the European price database EURIPID (European Integrated Price Information Database)[9]. The EURIPID collaboration is a voluntary cooperation between national competent authorities for pricing and reimbursement of medicines, whereby national prices of medicines are shared in a standardised format in the EURIPID database. The database contains data on official prices of publicly reimbursed medicines, predominantly in the outpatient setting, that are published by public authorities in line with the EC Transparency Directive (Council Directive 89/105/EEC 89\105\EC).

25. EURIPID data were used to support analysis of the survey domains (C) coverage and pricing, (D) treatment costs, and (F) utilisation. The database contains product-level information on the coverage status of (mostly outpatient) medicines at a defined period; package costs, based on ex-factory or retail prices; the existence of managed entry agreements; as well as some volume data. To the extent possible, data from the OECD survey were compared to that available in EURIPID.

1.3. Access indicators should also be viewed within the context of each country's health care system

26. As explained above, access is a multidimensional concept that is influenced by many factors, and any indicators used to measure or monitor access must be viewed within the context of each country's health care system. The policy-relevant context of health systems in the EU/European Economic Area has been extensively detailed elsewhere, such as in the *State of Health in the EU's Country Health Profiles*

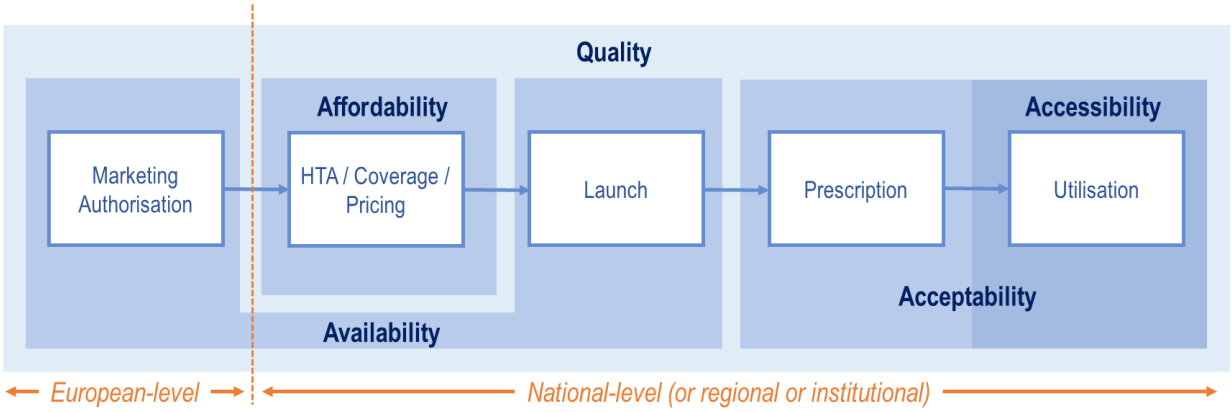
[8] Note that the situation (e.g. coverage) may have since changed in some countries.

[9] See https://euripid.eu/, last accessed 16 April 2022.

2021[10] and *Health at a Glance 2021*[11]. The pharmaceutical sector specific context has also been extensively explored and described, such as by the WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies through activities within the Pharmaceutical Pricing and Reimbursement Information (PPRI) Network[12] , and by the pharmaceutical industry (EFPIA, 2021[5]). More recently, a technical report produced as part of the Oslo Medicines Initiative presented a broad overview of some of the issues and complexities influencing affordability and accessibility to novel medicines within the European Region (Årdal, Lopert and Mestre-Ferrandiz, 2022[24]). While it is not possible to discuss all of these contextual factors in this paper, it is important to flag some of those that are most relevant.

27. Since 1995, the great majority of novel medicines in Europe have been subject to the centralised procedure of the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP), with subsequent decisions on marketing authorisation made by the European Commission. In Europe there is also a legal provision, known as the "sunset clause", which states that the "marketing authorisation of a medicine will cease to be valid if the medicine is not placed on the market within three years of the authorisation being granted or if the medicine is removed from the market for three consecutive years"[13]. All sample medicines included in the OECD survey were approved via the centralised procedure and have a current marketing authorisation, and thus the dimension of availability does not consider marketing authorisation. However, subsequent reimbursement decisions are the responsibility of competent authorities in individual Member States (see Figure 1.3).

Figure 1.3. In Europe, pricing and reimbursement is a national competence



Source: Authors.

[10] See https://www.oecd.org/health/country-health-profiles-eu.htm, accessed 18 April 2022.

[11] See https://www.oecd.org/health/health-at-a-glance/, accessed 18 April 2022.

[12] See https://ppri.goeg.at/PPRI_network, accessed 18 April 2022. The PPRI network is a collaboration of pharmaceutical pricing and reimbursement authorities of 50 largely European countries as well as international and European institutions. As part of its current work programme, the PPRI network is also developing a PPRI indicators portal, which will be a sustainable reporting system for meta-indicators to describe, measure and analyse pricing and reimbursement systems / policies across countries. There will be 67 indicators in total, organised within subcategories, covering structural, process, and results indicators. See Annex B of this report for further information.

[13] See https://www.ema.europa.eu/en/human-regulatory/post-authorisation/notifying-change-marketing-status, , accessed 9 October 2022.

28. The economic context, specifically in terms of spending on health and pharmaceuticals, differs greatly between European countries. In 2019, total health expenditure per capita in Europe ranged from EUR 1273 in Bulgaria to EUR 4661 in Norway, with an EU average of EUR 3521 (adjusted for differences in purchasing power). Relative spending as a share of GDP was more than two times higher in Germany (11.7%) than in Luxembourg (5.4%), with an EU average of 9.9%. In per person terms, spending on (outpatient) pharmaceuticals and medical devices in 2019 ranged from EUR 317 in Croatia to EUR 873 in Germany, with an EU average of EUR 630 (adjusted for differences in purchasing power). That same year, pharmaceuticals and medical devices absorbed between one-tenth (Norway – 10.2%) to more than a third (Bulgaria – 36.1%) of total health expenditure. In most EU countries, the bulk of health spending is publicly financed, but pharmaceuticals and medical devices constitute a large proportion of out-of-pocket costs for patients in some countries. As a share of total out-of-pocket costs, spending on outpatient medicines ranges from 16.6% in France to as high as 66.5% in Bulgaria (OECD/European Observatory on Health Systems Policies, 2021[25]).

29. **The way in which EU/EEA countries organise and finance their respective health systems differs substantially, which can influence measurements of patient access**. Reports published by Vogler et al. (2018[26]) and Vintura (2020[3]) outline some of these differences in detail – see Table 4.1 and Figure 4 in these publications, respectively. For outpatient medicines, most countries negotiate product prices and make reimbursement decisions at the national level. Decisions on reimbursement in the outpatient sector are commonly carried out by the ministry of health (or ministry of social affairs), or the social health insurance (SHI) fund (i.e. the umbrella organisation of the SHI institutions for SHI-based systems). For inpatient medicines, reimbursement decisions may also be carried out at the regional level (e.g. Austria, Denmark, Finland, Sweden). Funding for both outpatient and inpatient medicines is very complex in many countries, coming from health insurers – either a single payer institution or different health insurer – or at the regional or hospital level. Some countries, organise price negotiations, coverage decisions and funding on a national level, while others organise these different decisions at a partly national and partly regional level. In some countries, the same institutions are responsible for product pricing and coverage decisions, while in others specific institutions oversee coverage decisions. In several countries, both inpatient and outpatient reimbursement decisions are under the same competent authority, while practical decisions such as funding may be taken at a more decentralised level (Vogler et al., 2018[26]; Vintura, 2020[3]).

30. Coverage decision-making processes also vary according to the stakeholders and institutions involved, and countries manage their pharmaceutical benefit baskets in different ways. Most European countries apply a positive reimbursement list (also called a formulary), whereby all medicines included in this list can be prescribed and are paid for by the public payer (albeit with varying cost-sharing arrangements). Germany, however, applies a negative list i.e. specifies those medicines excluded from reimbursement. Here, all medicines entering the market are reimbursed by sickness funds unless they belong to a category excluded by law (e.g. over-the-counter) or by a decision of the Federal Joint Committee. Spain applies both a positive and negative list.

31. Many European countries have health technology assessment (HTA) mechanisms informing coverage decision-making for pharmaceuticals at national level – generally made up of either a singular national body, or two or more national HTA bodies (Chamova, 2017[27]). However, the HTA processes differ considerably from country to country, in the scope and role of HTA, the types of evaluations undertaken, and evidence requirements[14]. A comprehensive mapping exercise of HTA bodies in Europe

[14] See also IMPACT HTA's country vignettes on HTA appraisal/reimbursement processes for *rare disease treatments* https://www.impact-hta.eu/country-vignettes, accessed July 2022.

and Norway was published in 2017 (Chamova, 2017[27])[15]. In some countries, the same institution is responsible for HTA and coverage and pricing decisions (e.g. Austria, for outpatient medicines). In others, there may be no separate HTA agency or formal evaluation process, but instead the economic evaluation is undertaken along with the clinical part (e.g. Slovenia). Some countries do not have HTA processes (e.g. Iceland, Luxembourg), or have only recently introduced them (e.g. Greece, in 2018). A more recent report, commissioned as part of the Oslo Medicines Initiative, found that more than three-quarters (37 of 48) of countries in the WHO European region use HTA or HTA components to inform pricing and reimbursement processes medicines, with only 12 countries using HTA systematically (Vogler, 2022[28]). From January 2025, cooperation between European medicine regulators and HTA bodies will be governed by the Regulation on Health Technology Assessment (EU) 2021/228[16]. The Regulation establishes a mechanism via which any information, data, analyses and other evidence required for joint *clinical* assessment of health technologies is submitted by the pharmaceutical company only once at European level. It also defines rules and methodologies for joint clinical assessment of health technologies. The Regulation does not affect national competence to draw conclusions on the relative effectiveness of a health technology nor on national pricing and reimbursement decisions.

[15] See full report here: https://ec.europa.eu/health/system/files/2018-02/2018_mapping_npc_en_0.pdf and Annexes here: https://ec.europa.eu/health/system/files/2018-02/2018_mapping_npc_annexes_en_0.pdf . Note that this report is not just limited to pharmaceuticals. Accessed 19 April 2022.

[16] See https://health.ec.europa.eu/health-technology-assessment/regulation-health-technology-assessment/implementation-regulation-health-technology-assessment_en, accessed 09 October 2022.

2. Availability dimension: measures were difficult to interpret due to presence of confounders

32. This section explores some product/indication-level indicators of availability, using (non-representative) data from the OECD survey. It first examines counts or proportions of overall availability according to coverage status, followed by a more in-depth analysis into the breakdown of availability by presence of alternatives, progress within the coverage process (i.e. stage-in-process), and additional limitations on coverage (Section 2.1). Section 2.2 then presents an exploration into some differences in time-to-access estimates, followed by a cross-cutting analysis looking at the relationship between time-to-access and health spending (Section 2.3). The utility and feasibility of collecting and interpreting various data on availability are discussed throughout. Annex E presents additional analyses not included in the body of this paper.

2.1. Assessments of medicine availability should look beyond coverage status of individual medicines and reflect effective patient access to treatment

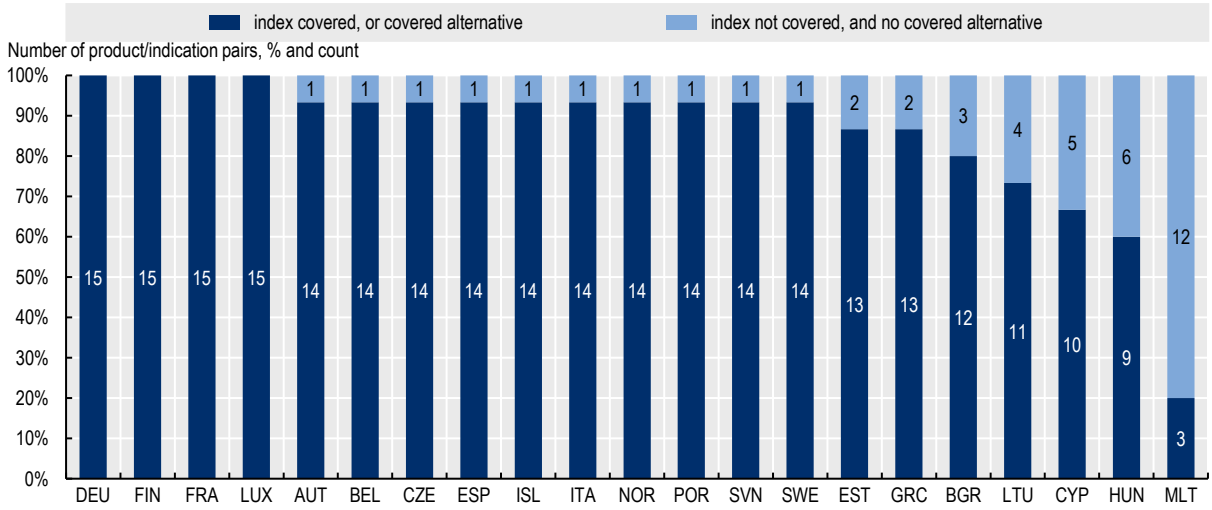
2.1.1. Availability estimates should consider presence of covered alternatives

33. Measures of availability of product/indication pairs in specific country markets are often presented by simple counts or proportions based on coverage status (e.g. inclusion in a reimbursement list) at a cross-sectional point in time, however, these figures can be misleading. Using basic counts, the number of covered index pairs as at 01 October 2021 in the OECD survey ranged from 0 in Malta, to the full 15 in Finland and Germany, with 14 countries reporting coverage of at least 80% of the sample (Figure AE.1, Annex E). However, the availability of treatment is augmented by the availability of alternatives. When taking into account the coverage of appropriate alternatives, either within class or within indication (see Table AE.1, Annex E, for a list of alternatives), country counts increased by an average of two pairs, and the order of countries by increasing availability changed slightly (Figure 2.1). Taking alternatives into account, the availability of medicines across the sample was more than 80% in the majority of responding countries (17 of 21). While considering alternatives may not appear to have a huge impact on overall availability in a small sample size, the effect in a larger, more representative, sample will be much greater. This is particularly pertinent in systems such as Malta, whereby both inpatient and outpatient products are purchased through centralised procurement processes and the availability of alternatives ensures competition. As such, measures of availability of treatment (as distinct from the availability of a product) should consider alternatives.[17]

[17] It is also important to recognise that only having information on coverage status does not indicate whether a medicine is readily available for pharmacists to dispense and patients to access, for example, due to medicine shortages.

Figure 2.1. Proportion of sample product/indication pairs by coverage status across countries

The availability of medicines across the sample was more than 80% in the majority of responding countries



Note: Proportions based on coverage status of a sample of 15 index product/indication pairs (or appropriate therapeutic alternatives), in 21 responding countries, as at 01 October 2021. Data labels show counts of product/indications (or alternatives) in each category, per country.
Source: OECD survey on access to novel medicines 2021.

34. Delving further into the access picture for individual medicines gives additional insight into the limitations of simple counts or proportions. For example, conclusions drawn may be more reflective of the medicine sample analysed (i.e. medicine-dependent) than the country situation (i.e. country-dependent) *per se*. Twelve of the fifteen index product/indication pairs in the sample were covered in at least two-thirds of responding countries (Figure AE.2, Annex E). The coverage picture improved when taking into account availability of appropriate alternatives, with 14 of the 15 index product/indication pairs in the sample covered in more than three-quarters of countries (Figure AE.3, Annex E). This additional analysis also indicates that availability of appropriate alternatives could contribute to lack of coverage of *niraparib* and *tivozanib*, as the number of countries covering these products increased from 12 to 19 and 5 to 21, respectively, when considering alternatives. However, the picture did not change for *asfotase alfa* as there are no alternative products available on the market. Section 2.1.2 gives further insight into reasons behind lack of perceived coverage of the sample products.

35. Furthermore, the year of the EU-wide marketing authorisation did not appear to influence the proportion of countries covering the index products (Figure AE.4, Annex E). This is unsurprising, as the sample products were all approved before October 2018, allowing at least 3-years between the EU-wide marketing authorisation and the cross-sectional cut-off date of 01 October 2021.

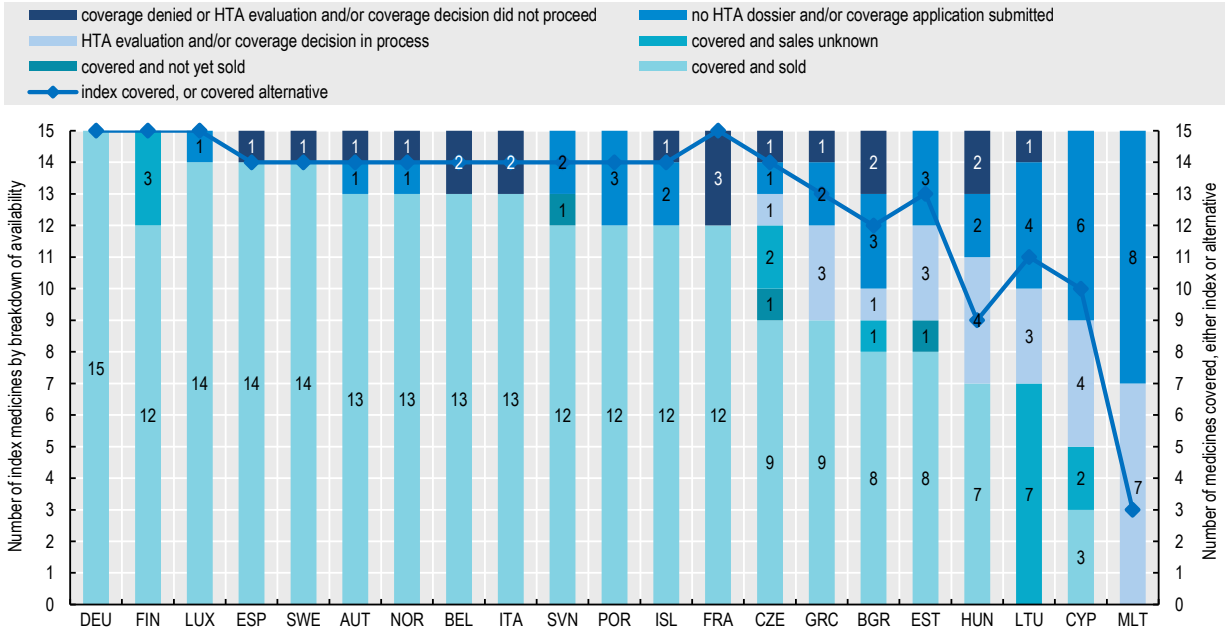
2.1.2. Availability estimates should take into account national HTA and coverage decision-making processes

36. Figure 2.2 below and Table AE.2, Annex E, provide a more comprehensive overview of availability across countries, and some insight into why medicines may not be covered at a particular point in time. They considered where a medicine was in terms of national HTA evaluation and coverage processes as at 01 October 2021, in addition to resulting coverage decisions and sales, as well as the availability of appropriate alternatives. Availability across the sample ranged from the greatest in Germany, whereby all product/indication pairs were covered and sold, to the lowest in Malta, whereby about half of the index products were either still undergoing HTA or coverage processes or no submission had yet been made.

Across the whole dataset of 315 country-product/indication pairs, the majority of sample products covered had been sold as at 01 October 2021. Out of a possible 315 cases, 26 (8%) were still undergoing HTA evaluation or a coverage decision, 39 (12%) had not yet had an HTA or coverage application submitted, and 19 (6%) had a negative coverage decision or the HTA or coverage process did not proceed. In the majority of cases whereby an HTA dossier had not yet been submitted, the company had not indicated to the country its intention to submit (or not) an application (see further details below). Malta was the country with the highest number of both submissions in process or no submissions made, followed by Cyprus, Lithuania, and Hungary. Considering the availability of alternatives, these four countries still appeared to have the lowest total availability across the sample.

Figure 2.2. Proportion of sample product/indication pairs by availability breakdown across countries

Availability breakdown by stage-in-process provided further insight into the access situation



Notes:
Left-hand vertical axis: bars represent breakdown of availability of a sample of 15 index product/indication pairs, in 21 responding countries.
Right-hand vertical access: blue line shows number of covered products (either index or alternative). As at 01 October 2021.
The number of covered products – either index or alternative – on the right-hand vertical axis has no relation to the breakdown of availability categories shown in the columns on the left-hand axis. It is included to show that the overall availability in a country cannot be reflected by coverage of the index product/indication pairs alone.
Example of how to read the graph: Twelve of the index product/indication pairs are covered in France. This number increases to 15 when considering covered alternatives.
Source: OECD survey on access to novel medicines 2021.

37. Figure AE.5 and Table AE.2, Annex E, provide further insight into the access picture for individual medicines. For example, *tivozanib* and *asfotase alfa* were not brought to market (i.e. no HTA dossier and/or coverage application was submitted) as at 01 October 2021 in 10 and 11 countries, respectively, with 5 countries denying coverage for each product. One country denied coverage for *tivozanib* because the condition to be paid by public funds in a certain number of other EU countries was not met. Another country deemed the product not essential for the national health system due to safety issues and low efficacy. However, an appropriate alternative to *tivozanib* was available in all countries in which the product was not covered, suggesting that patients were not disadvantaged due to lack of access to *tivozanib* specifically.

Asfotase alfa, on the other hand, is an ultra-orphan product with no alternatives and was only covered in four countries despite receiving an EU-wide authorisation in 2015. In some countries, applications for population-wide coverage may not be made for products used in the treatment of very rare diseases, or where the predicted demand is likely to be small (Box 2.1), which is often the case for smaller markets, such as Malta and Lithuania.

38. It is worth noting that while some of these product/indication pairs were not covered as at 01 October 2021, they may have been covered through other means for a small number of patients. For example, in Greece, *asofatase alfa, edoxaban, niraparib* and *tivozanib* were covered on a named patient basis (with prior authorisation). In Malta, *alirocumab, mepolizumab* and *ocrelizumab* were available through a similar process. While data on alternative access mechanisms were not directly collected through the OECD survey, Box 2.1 describes some examples. Box 2.2 includes additional information about early access schemes that was collected via the OECD survey, however information was not collected about whether schemes were named-patient versus population-based.

39. The survey data allowed for further exploration into HTA and coverage processes, although results have limited meaning given that they may reflect either country-dependent or medicine-dependent issues from a small sample size. Nevertheless, across the whole dataset of 315 country-product/indication pairs, in most cases whereby an HTA dossier was not submitted, the company had not indicated to the country its intention to submit (or not) an application (34 of 37). Of those 215 cases for which an HTA dossier had been submitted, more than 90% (201 of 215 cases) had been completed, with 7% (14 of 215) not yet complete. Of those 14 cases for which an HTA dossier had not yet been completed, in 9 the dossier was under evaluation, in 4 other, and in 1 the HTA could not proceed.

Box 2.1. Some countries use alternative access mechanisms to provide or accelerate access to certain medicines

As described by Németh et al. (2022[29]), lack of inclusion in a positive reimbursement list does not necessarily imply lack of patient access *per se*, particularly in low and middle income countries. For example, alternative mechanisms may provide a small, intended treatment population with access to high-priced medicines on a named-patient basis. Respondents to the OECD survey flagged this point being particularly relevant in the case of small markets for which lack of access could also be the result of little (or unpredictable) demand. This is likely to be the case for advanced therapy medicinal products (ATMPs), orphan/ ultra-orphan products but also certain other products with very small patient populations. Some examples are:

- **Malta:** The **named-patient basis** process, formally known as the Exceptional Medicinal Treatment Policy (EMTP), is an established process that provides access to treatment outside of what is included in the Government Formulary List. Only medicines for certain diseases or conditions are reimbursed, which is governed by the Fifth Schedule of the Social Security Act. The EMTP pathway allows patients access to: a medicine not listed on the Government Formulary List; listed on the Government Formulary list but not according to protocol, indication or prescribed criteria; specifically branded medicines; or medicines for the treatment of rare diseases. Individual patient requests are submitted by physicians and evidence is assessed by the Exceptional Medicinal Treatment Committee.[1]
- **Greece:** While some medicines may not be included in a positive reimbursement list, reimbursement may still be possible on a case-by-case basis after prior authorisation (i.e. via **named-patient programmes**).
- **Cyprus:** The Ministry of Health has its own committee which may reimburse patients on a **name basis.**
- **Lithuania:** Decisions on medicines intended for the treatment of very rare diseases will only be made for **individual patients**, on a case-by-case basis.

- **Austria:** According to the Austrian General Social Security Law, a product that is not (yet) covered can be prescribed to an insured person in justified individual cases if the treatment is necessary for compelling therapeutic reasons and therefore the prescription in these individual cases cannot be carried out with products from the positive reimbursement list (i.e. prescription on an **individual case-by-case basis**). If alternatives exist, they should be prescribed primarily.

In some countries early access schemes are used as an alternative access mechanism to accelerate access to a limited number of patients – either to individual patients (named-patient programmes) or groups of patients (population-based programmes) – at the initial stages of the lifecycle of a medicine, prior to inclusion in a positive reimbursement list (see Box 1.2 for further details). While the majority of these schemes focus on very small patient populations or patient numbers with specific restrictions on use, some countries have established mechanisms to accelerate access to broader patient populations. Examples of the early access systems in Portugal and France are described below. Box 2.2 provides further exploration of early access schemes as collected in the OECD survey.

- **France:** France has well-established mechanisms to fund **early or exceptional access** to some medicines. L'autorisation temporaire d'utilisation (ATU) – introduced in 1992 - allowed use of medicines likely to be innovative and meet an unmet therapeutic need prior to marketing authorisation and throughout the evaluation process, either on an individual-basis or for a cohort of patients. Since July 2021, previous early access schemes have been reformed and replaced by two schemes: (1) the "early access" program, (population-based) for supposedly innovative medicines addressing unmet medical needs and for which the company commits to file a marketing authorisation or apply for coverage under the common procedure – referred to in this paper as "early access coverage schemes"; and (2) the "compassionate access" (name-based) for medicines that are not necessarily innovative, which are not initially intended to obtain a marketing authorisation but that satisfactorily address an unmet medical need (Assurance Maladie, 2022[30]).
- **Portugal: Early access schemes** are used to provide access during the time that a medicine is assessed, and a price negotiated, particularly for medicines without an alternative or that treat a serious and life-threatening condition. While early access is approved on a case-by-case basis, this type of programme is open to the intended treatment population. Patients generally receive the medicine free of charge. There are also mechanisms in place to ensure access to medicines prior to marketing authorisation, in specific situations.

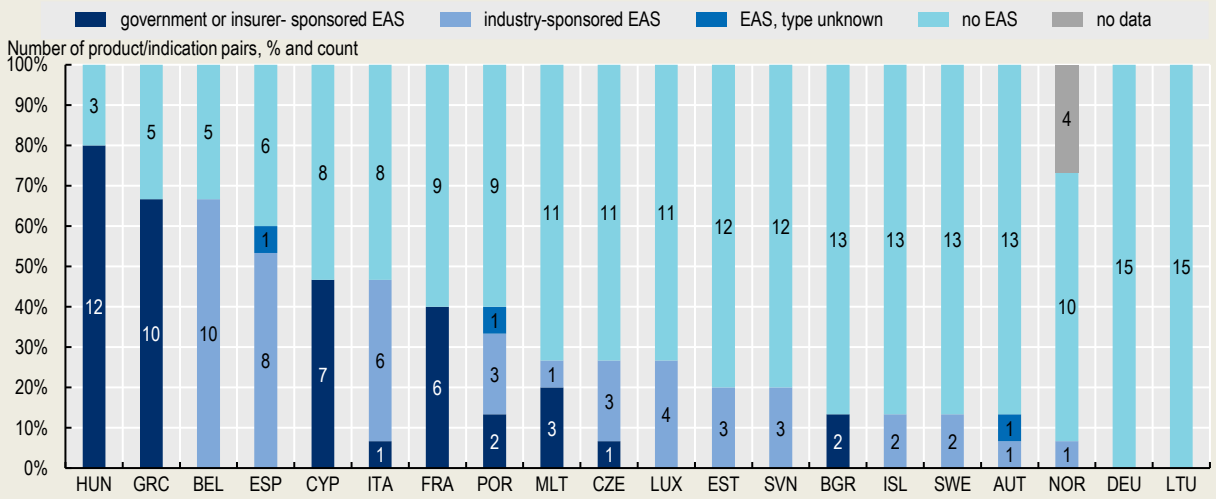
Source: OECD survey and discussions with Experts 2021. 1. See Legal Notice 58 of 2018, as amended by Legal Notice 448 of 2018 regarding the Exceptional Medicinal Treatment Committee Regulations https://legislation.mt/eli/sl/528.8/eng and the circular issued by the Office of the Chief Medical Officer concerning the Exceptional Medicinal Treatment Policy and associated Schedule of Review Criteria for assessment of Exceptional Medicinal Treatment Requests https://deputyprimeminister.gov.mt/en/pharmaceutical/Documents/Circulars/2019/circular_22_2019.pdf, accessed July 2022.

Box 2.2. Although not a measure of general patient availability, most responding countries were able to provide data on early access schemes

Survey respondents were asked whether there was (or had been) an early access scheme (EAS) for the index product/indication pairs as at 01 October 2021. As explained in Box 1.2, these schemes may allow temporary access to medicines either prior to the marketing authorisation or prior to the publicly funded coverage decision. In general, they apply to therapies used in severe diseases with high unmet need. The existence of EAS varied across countries and across product/indication pairs – see Figure 2.3 below and Figure AE.6 and Table AE.3, Annex E. Germany and Lithuania did not report EAS for any of the product/indication pairs, while Hungary, Greece, and Belgium reported an EAS for at least 10. Most countries used predominantly one type of funding arrangement. *Ocrelizumab* and *nusinersen* had an EAS in the highest number of responding countries (14 and 12, respectively), while *semaglutide* and *edoxaban* did not have an EAS in any country. Different types of EAS funding arrangements were employed for the same product across countries.

Figure 2.3. Proportion of sample product/indication pairs by early access scheme across countries

Use of early access schemes varied across countries



Note: Proportions based on a sample of 15 index product/indication pairs, as at 01 October 2021. Data labels show counts of product/indication pairs. In Finland, some pharmaceutical companies may use EAS, but there is no public data. Germany may have EAS under special circumstances whereby the pharmaceutical company provides the medicinal product prior to marketing authorisation on a voluntary basis. Source: OECD survey on access to novel medicines 2021.

Further analyses into the relationship between EAS and resulting coverage decisions were made by looking at the whole study dataset (315 country-product/indication pairs), but the results are by no means representative. Early access schemes had existed in under a third of cases where the product was covered, and also in a similar proportion where the product was not covered. For those 94 cases in which an EAS existed, less than half were in place prior to central marketing authorisation, almost all in place prior to a publicly funded coverage decision, and around a quarter were continued after a coverage decision. Around half of the EAS in place were industry-funded, with the other half sponsored by governments or insurers.

Although data on EAS may be of interest to policy makers, in general, information on their existence is not readily publicly available, which challenges routine collection. Some countries publish a list of active programs (e.g. Austria, Belgium, France, Portugal, Sweden), but retrospective data are not readily available in the public domain. In some cases, the existence of an EAS may be inferred by sales data prior marketing authorisation (e.g. Iceland). Particularly in the case of industry-sponsored schemes, it is unsurprising that data may be difficult to obtain directly from countries. Nevertheless, the relationship between the existence of EAS and other variables, such as the availability of alternatives, severity and type of disease, and time to coverage decision warrants further exploration.

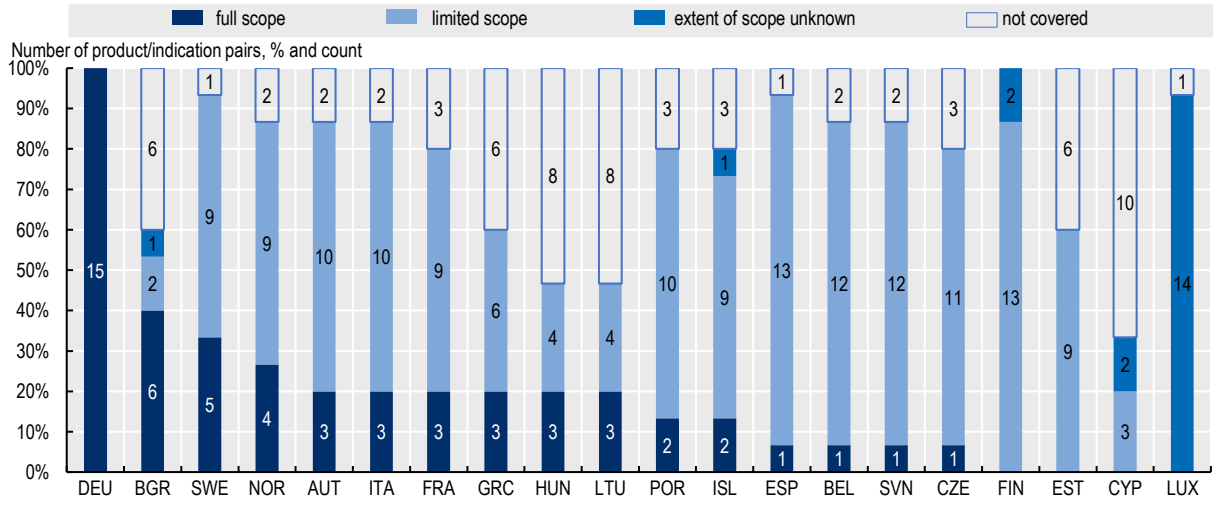
Note: No information was collected in the OECD survey about whether EAS were named-patient versus population-based programs.
Source: Authors based on results of the OECD survey on access to novel medicines 2021.

2.1.3. Availability estimates should also consider any limitations in coverage

40. Exploring the breakdown of covered products by the extent of coverage in comparison to the approved indication provides yet further insight into patient access within country markets. Except for Germany and Bulgaria, most survey respondents reported limitations in the scope of coverage relative to the EU authorised indication for most of their respective covered products by at least one of the following: (1) characteristics of the patient population or subgroup, (2) duration or quantity of treatment for individual patients, or (3) pre-requisite of failure of (or intolerance to) a prior therapy (Figure 2.4). The trend in extent of coverage appeared to be similar across medicines, with coverage limited in scope in comparison to the EU indication in most countries (see Figure AE.7 and Table AE.4, Annex E). The coverage of *sacubitril/valsartan* was limited in scope in the most number of responding countries (Figure AE.7, Annex E). Across the whole sample of 231 covered country-product/indication pairs, around two-thirds reported narrower coverage than the EU authorised indication by (1), about half by (3), and less than a quarter by (2). This suggests that both (1) and (3) might be useful categories with which to measure extent of coverage in comparison to the marketed indication.

Figure 2.4. Proportion of sample product/indication pairs by extent of coverage in comparison to the authorised indication across countries

Most countries limited the scope of the covered indications relative to the EU approved indications for marketing - by patient population, treatment duration, or place in therapy



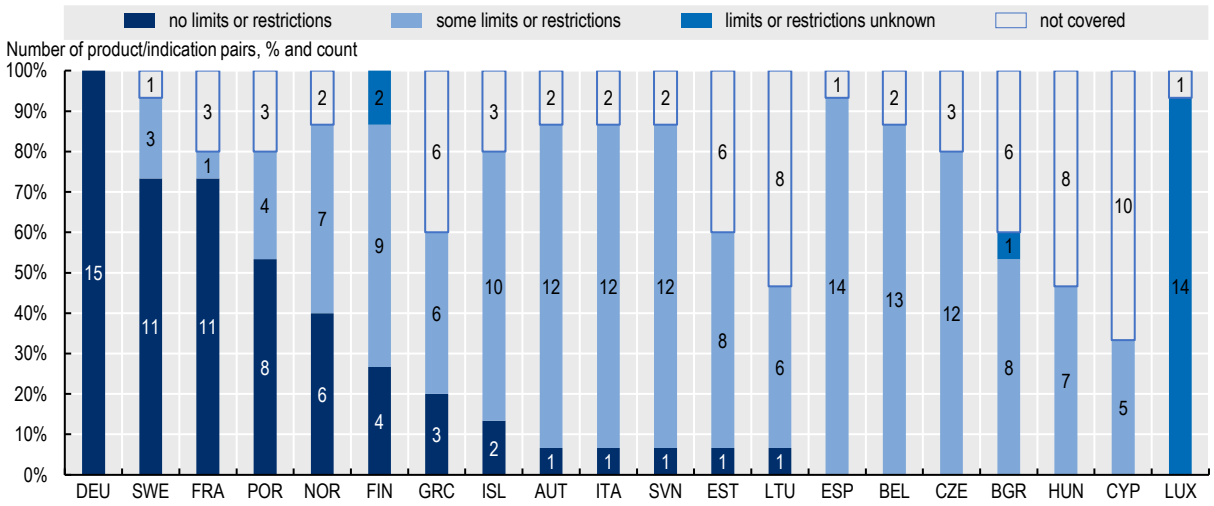
Note: Proportions based on sample of 15 index product/indication pairs, in 21 responding countries, as at 01 October 2021. Data labels show counts of product/indications in each category, per country. Full scope = covered indication not narrower than the EU authorised indication by (1) patient population or subgroup, (2) duration or quantity of treatment for individual patients, or (3) prerequisite of failure of (or intolerance to) a prior therapy. Limited scope = covered indication narrower than the EU authorised indication by at least one of categories (1), (2) or (3). Malta was excluded as no product/indication pairs were covered.
Source: OECD survey on access to novel medicines 2021.

41. Similarly, exploring additional limitations and restrictions in coverage can highlight disparities in patient access. Germany, Sweden, France, and Portugal did not place additional limits or restrictions in coverage for more than two-thirds of their respective covered products (Figure 2.5). Most other countries with available data applied at least one of the following limits or restrictions for most products: (1) requirements to demonstrate a pre-determined response to treatment; (2) maximum number of patients eligible for treatment per annum; (3) limited to prescriber type; or (4) other. The other category included, for example, restrictions on use in combination and requirement of prior non-pharmacological measures. Several countries almost exclusively reported some limits or restrictions. All products had coverage limits

applied in at least two countries, with most products having limits applied in more than 10 countries (see Figure AE.8 and Table AE.5, Annex E). Across the whole sample of 231 country-product/indication pairs, around 60% were reported as restricted by (3), over 30% by (4), around 20% by (1) and less than 5% by (2).

Figure 2.5. Proportion of sample product/indication pairs by additional limits and restrictions in coverage across countries

Most countries applied additional limits or restrictions to coverage decisions - by treatment response, number of patients, prescriber type, or other restrictions



Note: Proportions based on sample of 15 index product/indication pairs, in 21 responding countries, as at 01 October 2021. Data labels show counts of product/indications in each category, per country. No limits or restrictions = coverage not restricted by (1) requirement for demonstrated response to treatment; (2) maximum number of patients per annum; (3) prescriber type; or (4) other. Some limits or restrictions = coverage restricted by at least one of categories (1), (2), (3) of (4). Malta was excluded as no product/indication pairs were covered.
Source: OECD survey on access to novel medicines 2021.

42. Although these figures cannot be considered representative of the situation within countries given the small non-representative sample, they highlight the need to consider the effect of limitations and restrictions in coverage and resulting patient access. Only 32 of 231 covered country-product/indication combinations fulfilled the abovementioned requirements of both “full scope” (Figure 2.4) and “no limits or restrictions” (Figure 2.5), as explored in this study.

2.1.4. The presence of confounders and the administrative burden of data collection present challenges for the generation and interpretation of routine availability metrics

43. **While all responding countries were able to report data on coverage status, the availability of this information in the public domain varied, and collecting nationally representative data can be challenging**, particularly for hospital products. Detailed data on coverage decisions are relevant for those countries that use a positive list(s) (i.e. inclusion of a product on a formulary), but not applicable for those with a negative list (Table 2.1). Most countries with a positive list(s) publish information on national coverage status of medicines, however this is generally only publicly available once a coverage decision has been made. Some countries have more than one list, for example for inpatient versus outpatient medicines. These may be in the form of downloadable PDF or Microsoft Excel files or a searchable database in which information can only be viewed for one medicine at a time. However, not all lists include

information on the indication for which the medicine is reimbursable. In some countries, decisions on reimbursement, particularly for inpatient products (e.g. Sweden), are decentralised and there are no definitive national decisions made on coverage and pricing. In other cases (e.g. Cyprus, Malta, Norway), some products may be procured competitively within class, rather than through an individual process. Collaborative platforms, such as EURIPID, could aid more routine collection and analysis as it collates public information on reimbursement status of medicines across member countries – however, data pertains to mostly outpatient medicines, and information on the reimbursable indication is not present.

Table 2.1. Type of reimbursement list used by countries in the outpatient sector

Most of the 21 responding countries use positive reimbursement lists (i.e. formularies) in the outpatient sector

Type of reimbursement list	Countries
Positive (N=19)	Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Estonia, Finland, France, Greece, Hungary, Iceland, Italy, Lithuania, Luxembourg, Malta, Norway, Portugal, Slovenia, Sweden
Negative (N=1)	Germany
Both (N=1)	Spain

Source: Authors, based on (Vogler et al., 2018[26]) and OECD survey 2021.

44. **Breaking down availability by stage-in-process and looking beyond coverage status is desirable, but adds data collection challenges**. Here, and as outlined in the above sections, stage-in-process refers to where a product/indication pair is at a given point in time in terms of HTA and/or coverage decision processes (see Figure 2.2, for example). In this analysis, this information was drawn from several survey questions (see example survey questions in Table AD.2, Annex D). However, a difficulty arises as, with the exception of Belgium and Portugal, the data are often not centralised across processes and hence not easily retrievable even by local experts within a country, nor are they necessarily publicly available.

45. As already foreshadowed in Section 1.3, **countries also vary considerably in their HTA and coverage decision-making processes, which may be carried out by different institutions, complicating data collection** (see Table AE.6, Annex E, for further details). Data collection issues related to coverage processes have already been outlined above. Regarding HTA, data are not generally publicly available unless a report has been completed and published. In some countries HTA reports are not made public (e.g. Austria), and others only publish information on the final outcome / opinion and not the full report (e.g. Bulgaria, Greece, Hungary). In some countries, HTA is decentralised (e.g. Sweden for inpatient medicines), and in others there is no formal national HTA process (e.g. Iceland, Luxembourg) or one has only been introduced recently (e.g. Greece, Lithuania). As with coverage decisions, there may also be applications made for groups rather than individual products (e.g. Estonia). Existing collaborative platforms such as the INAHTA database do collate information about ongoing and published health technology assessments, but data coverage may be inadequate for a routine exercise[18].

46. **Considering the availability of alternatives when measuring access at the product/indication-level is essential, but also brings additional challenges**. The OECD survey collected information on alternatives in a rather simplistic manner: if not covered, is there another covered product, either within the same, or from another therapeutic class considered to be a satisfactory alternative, and if so, to provide the name. This information was mainly used to qualify the availability results for the study sample, acknowledging that while broad access to all medicines may seem ideal, it may not in fact be essential (see Section 5. for further details). Collecting basic coverage status information on alternatives faces the same challenges as already described above. In addition, countries may consider different alternatives as appropriate, depending on their specific contexts. However, such a simplistic view

[18] See https://database.inahta.org/, accessed October 2022.

does not allow a further breakdown of availability to alternatives, nor does it really consider the appropriateness of said alternatives. Should further work continue at this level, consideration should be made on how best to account for alternatives in the context of routine collection, as well as agreeing on the appropriate alternatives for each medicine *a priori*.

47. **Collecting data on any limitations or restrictions in the covered indication can further highlight disparities in access across countries, although it adds an additional administration burden**. As described in Section 2.1.3, this survey asked whether or not the reimbursed or covered indication was narrower than the marketing authorisation indication by (1) patient population or subgroup, (2) duration or quantity of treatment for individual patients), and (3) pre-requisite of failure of (or intolerance to) a prior therapy. The survey also asked whether any of the following restrictions applied: (1) requirements for demonstrated response to treatment, (2) maximum number of patients eligible for treatment per annum, (3) prescriber type, and (4) other. Detailed data to answer these questions are not readily available in a standardised format and references to original documents are required to clarify details. Despite this, most countries were able to respond to at least one, if not all, of these questions for most covered products. No data were available for Luxembourg. To be pragmatic, any desired further work should attempt to clarify the key elements of most interest with regard to defining coverage limitations, and how to best ensure comparability.

2.2. Decomposing time-to-access offers insight into access bottlenecks, although early access coverage was not considered in this analysis

2.2.1. Measurements of time-to-access obscure the decomposition of the various time periods between marketing authorisation and patient access

48. **For comparisons among countries within Europe, the most pertinent measures of time-to-access begin from the date of the EU-wide marketing authorisation.** As mentioned above, all 15 sample product/indication pairs were authorised via the centralised procedure (explained further in Section 1.3 and Annex E) and thus the marketing authorisation date is the same across countries. Indeed, while marketing authorisation is the first step in market access, in many countries, companies may choose to launch a medicine only once it has coverage (often at a regulated price) or to delay it because of the extensive use of external price referencing. There are some exceptions: in Germany for example, every authorised medicine is initially covered by default, and companies generally introduce products to market at the same time as the first HTA application. In some countries, a product may also be supplied prior to a coverage decision, generally on a case-by-case basis but sometimes wider population-access is also possible (see Box 1.2, Box 2.1, Box 2.2, and in Section 2.2.2).

49. **Existing measurements of time-to-access obscure the decomposition of the various time periods that occur between marketing authorisation and patient access** (see examples of decomposed time periods in Table AC.2, Annex C). Usually, time-to-access (or availability) differences between countries are presented as averages (or associated ranges) between marketing authorisation and granting of coverage (or inclusion in a reimbursement list) across available products in each market. However, these estimates do not provide insight into why patients might gain access to the same medicine sooner in some countries than in others. As such, the OECD survey explored some sort of decomposition as described in Annex E, although **data were incomplete and cannot be considered representative of the access situation in individual countries**.

50. The total time between marketing authorisation and a national positive coverage decision[19] is first presented below (Figure 2.7), and then decomposed into several periods:

- **Period 1:** marketing authorisation to either first HTA or coverage application (Figure 2.8)
- **Period 2:** first HTA application to first coverage application (graph not shown)
- **Period 3:** first coverage application to first positive coverage decision (Figure 2.9)
  - **Period 3a:** first successful coverage application to first positive coverage decision, without considering clock stops (Figure AE.11, Annex E)
  - **Period 3b:** first successful coverage application to first positive coverage decision, considering clock stops for subset with available data (Figure 2.10)
- **Period 4:** positive coverage decision to first sale (Figure 2.11)

51. While these are the only time periods discussed in this paper, others could be further explored. For example, it would be interesting to examine the breakdown of the health technology assessment process, or the role of pricing decisions. The latter is particularly pertinent when reimbursement and pricing decisions are interlinked. In addition, the impact of early access schemes could be explored, particularly in the case of "early access coverage schemes", which are defined in this paper as publicly funded population-based programmes that benefit the entire target population within an indication (see Box 1.2). The time difference calculations in this paper do not account for these schemes, meaning the time to patient access could be shorter in some countries. For example, measuring time-to-access in France without taking into account these population-wide schemes can be misleading (Assurance Maladie, 2022[30]). Although comprehensive data was not collected in the OECD survey about the specific types of early access schemes used by countries, each of the time difference graphs are supplemented by counts of products (from those with available dates) granted some form of early access.

52. Box plots are used below to display the distribution in time differences within countries for the small, heterogenous sample dataset. It is important to note that **time-to-access may be over- or underestimated depending on the sample chosen and system of measurement (i.e. metrics) used**. For example, simple averages are dependent on both the *number* of medicines covered in each country market (which can vary significantly) as well as on *which* medicines are covered – both of which can skew the result. Box 2.3 further outlines some of these considerations. Consequently, ***medians* are used here to depict comparisons given that they are less susceptible than averages to outliers.**

[19] It is recognised that the national coverage decision date is not necessarily the same date as actual coverage i.e. when a product is included in a positive reimbursement list or available to be prescribed in a national pharmacy database. This date was chosen for practical reasons and can be considered as a proxy of coverage date. It is also important to recognise that time-to-access as measured in this study does not measure time limit delays as defined in the Transparency Directive (directive 89/105/EC). This time period also does not account for population-wide early access schemes that may be used to accelerate access in some countries, meaning the time difference displayed could be shorter for some countries.

Box 2.3. Time-to-access may be over- or under- estimated depending on the sample chosen and metrics used

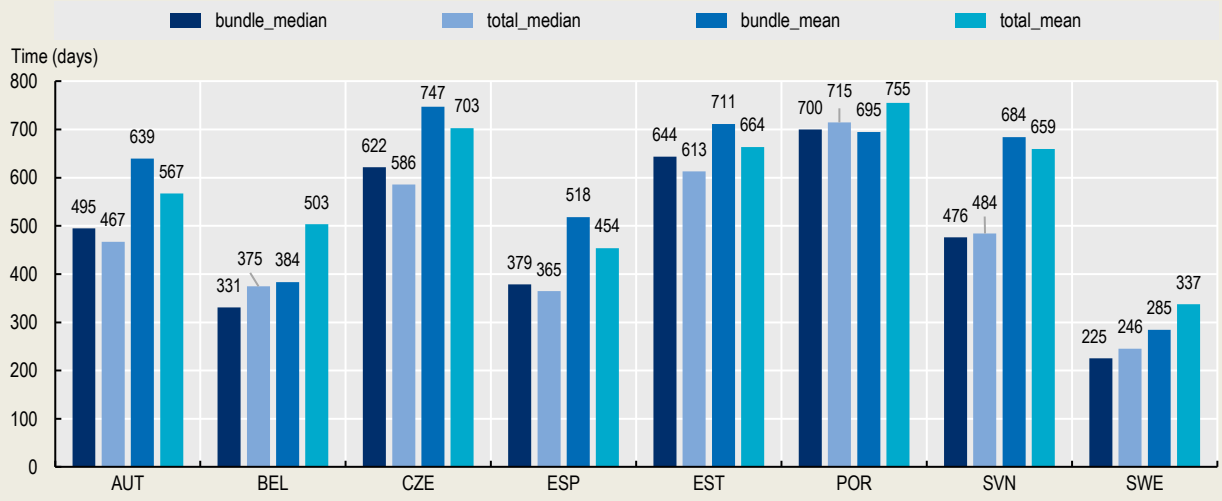
Time-to-access (or availability) differences may be over- or under- estimated depending on the analysis sample chosen and system of measurement used. Simple averages depend on both the *number* of medicines covered in each country market (which can vary significantly) as well as on *which* medicines are covered – both of which can skew the result. For example, if an average is presented for a country calculated using data for a few products, for which the time to coverage is longer than for other products, this may overestimate the time difference for this country. Figure AE.10, Annex E, shows that the average time from marketing authorisation to a positive coverage decision varied significantly between the 15 sample pairs, from around 350 days for *sofosbuvir/velpatasvir* and more than 800 days for *edoxaban*. Variations in this time period are driven by several factors, however, and they can be misleading if given alone – for example, they do not consider company launch strategies nor the effect of multiple (failed) submissions.

Given that these time differences may reflect *medicine-dependent*, rather than *country-dependent* trends (particularly given the small sample size in this study[1]), time between marketing authorisation and positive coverage decision was analysed by first looking at the whole sample and then again using a bundle of eight product/indication pairs for which there were the same data points in multiple countries. Both average and median time differences varied across the bundle and the total sample, and country order from shortest to longest time differences also changed (Figure 2.6). Although calculating values using the same medicines in all countries should theoretically provide a more comparative picture of time differences in access, this can also be skewed if an individual product/indication pair was an outlier for any reason. This was likely the case for *mepolizumab* in Spain, and *edoxaban* in Slovenia, for example.

Previous research on time-to-access differences across countries mainly used average as a metric, however, due to the small study sample median was preferred as it is less susceptible to outliers. Figure 2.6 shows that averages for both the bundle and total sample are significantly higher than the medians for several countries, signalling the presence of outliers in both samples. Moreover, an assessment of the homogeneity of time-to-access processes in each country could be of interest, for example by looking at a measure of variability such as the interquartile range of a sample.

Figure 2.6. Time between EU marketing authorisation and positive coverage decision, total and bundle sample, in days (excluding early access coverage schemes)

Time difference measurements can be skewed by the product sample chosen for analysis and metrics used



Note: Shows time between EU marketing authorisation and positive coverage decision for total and bundle sample using median and average (mean). Bundle of eight medicines: *baricitinib, dupilumab, edoxaban, mepolizumab, palbociclib, sacubtril/valsartan, semaglutide sofosbuvir/velpatasvir.*

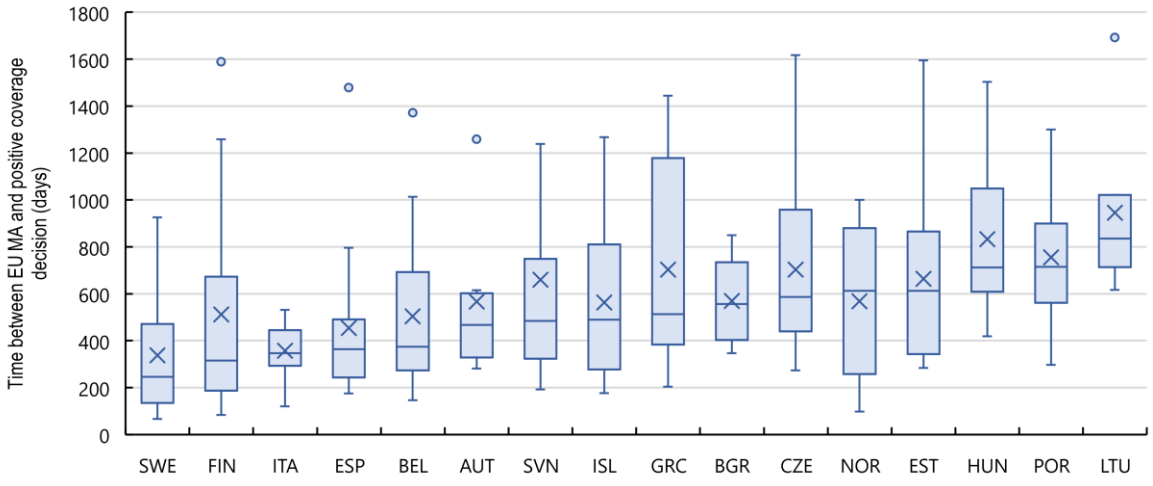
1. With a larger sample size and greater data availability, the use of more sophisticated statistical methods could provide better insights into medicine-dependent versus country-dependent issues.

Source: Authors, as cited. OECD survey on access to novel medicines 2021

53. Despite these limitations in data comparability and interpretation, the **median time between marketing authorisation and positive coverage decision** (early access coverage excluded) **for most responding countries fell within a one-to-two-year time frame** (11 of 16 responding countries, see Figure 2.7). It ranged from less than 12 months in Sweden, Finland, Italy, and Spain, to more than 2 years in Lithuania. However, even within a country, the time differences varied widely among products, with some considerable outliers. For example, in Slovenia, the difference ranged from about 6 months to more than 6 years, while in Italy it ranged from around 4 months to 1.5 years. The box plots are useful to show the large dispersion of data within the sample. For most countries, the data were positively skewed i.e. the median was closer to the bottom quartile, meaning that data constituted a higher frequency of high valued scores.

Figure 2.7. Time between EU marketing authorisation and positive coverage decision, in days (excluding early access coverage schemes)

The time between EU marketing authorisation and positive coverage decision ranged from one to two years for most countries



	SWE	FIN	ITA	ESP	BEL	AUT	SVN	ISL	GRC	BGR	CZE	NOR	EST	HUN	POR	LTU
No. covered	*14*	*15*	*13*	*14*	*13*	*13*	*13*	*12*	*9*	*9*	*12*	*13*	*9*	*7*	*12*	*7*
Available dates	*12*	*13*	*12*	*14*	*13*	*12*	*13*	*11*	*9*	*8*	*11*	*11*	*9*	*7*	*12*	*7*
- No. with EAS	*1*	*0*	*5*	*8*	*9*	*1*	*3*	*1*	*5*	*1*	*3*	*1*	*3*	*5*	*6*	*0*

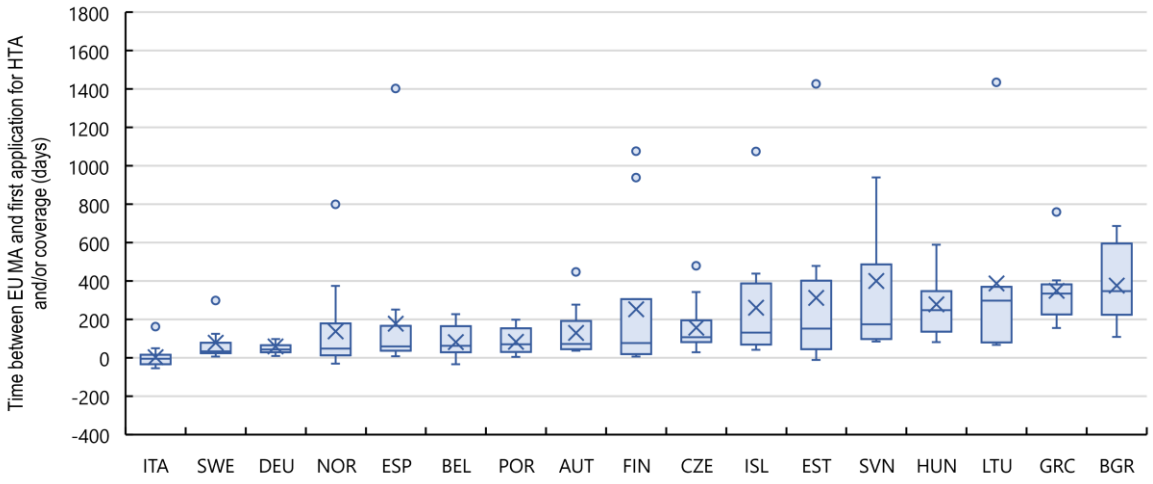
Note: X = average time in days per country, across the count of product/indication pairs; MA = marketing authorisation; EAS = early access scheme, either named-patient or population-based (see Box 2.2, and Table AE.3 in Annex E). Outlier of 2320 days for Slovenia not shown.
Based on *covered* products with available date information, from a non-representative convenience sample of 15 product/indication pairs. The product/indication pairs for which these time periods are computed differs among countries. In Germany, every authorised medicine is initially covered by default, and companies generally introduce products to market at the same time as the first health technology assessment application (see Figure 2.8). The time difference calculations do not account for population-wide early access schemes that may be used to accelerate access in some countries, meaning the time difference displayed could be shorter for some countries.
Source: OECD survey on access to novel medicines 2021.

54. However, **decomposed time periods show that some countries wait longer than others for manufacturers to make an application for HTA or coverage of a product**. Over half of the seventeen responding countries with available data received an application within three months of EU marketing authorisation, four countries between three and six months, while Hungary, Lithuania, Greece, and Bulgaria waited between six months to a year. Again, there were large variations in the spread of data within the sample, with several outliers, skewing the results. In Estonia for example, there was a difference of more than four years between this calculated time for two product/indication pairs. As described previously, differences between countries in this indicator may reflect launch strategies of pharmaceutical

companies (i.e. sequential product launches and delayed application for coverage/pricing decisions influenced by market size and national pharmaceutical policies). To accelerate access, some countries allow companies to submit HTA and or coverage applications before the product receives marketing authorisation, or employ early access mechanisms (see Section 2.2.2 and Box 2.2).

Figure 2.8. Time between EU marketing authorisation and first application for HTA and/or coverage, in days (Period 1)

Some countries waited longer than others for manufacturers to make an application for HTA and/or coverage



	ITA	SWE	DEU	NOR	ESP	BEL	POR	AUT	FIN	CZE	ISL	EST	SVN	HUN	LTU	GRC	BGR
No. covered	13	14	15	13	14	13	12	13	15	12	12	9	13	7	7	9	9
Available dates	13	14	15	13	14	13	12	12	12	12	11	8	13	7	7	9	8
- No. with EAS	5	2	0	1	8	9	6	1	0	4	1	3	3	5	0	5	1

Note: X = average time in days per country, across the count of product/indication pairs. MA = marketing authorisation; HTA = health technology assessment; EAS = early access scheme, either named-patient or population-based (see Box 2.2, and Table AE.3 in Annex E). Outlier of 1866 days for Slovenia not shown.
Based on *covered* products with available date information, from a non-representative convenience sample of 15 product/indication pairs. The product/indication pairs for which these time periods are computed differs among countries.
Source: OECD survey on access to novel medicines 2021.

55. **HTA and coverage applications were filed simultaneously in most responding countries, either because it is a joint process, or within the same institution** (see Table 2.2). Given this, and that HTA and/or coverage is not applicable in some countries, the figure for this period is not shown. Nevertheless, this time difference among products even within one country varied widely. Long delays here likely reflect more than one submission for HTA.

Table 2.2. Timing of HTA and coverage applications in responding countries

HTA and coverage applications are filed at the same time in most responding EU Member States

	Countries
HTA and coverage filed at the same time (i.e. because it is a joint process, or within the same institution) (N=13)	Austria, Belgium, Bulgaria, Czech Republic, Estonia, Finland, Greece, Hungary, Italy, Norway, Portugal, Slovenia, Sweden
HTA and coverage may be filed at different times (N=2)	France, Spain
No (common) HTA evaluation (N=3)	Iceland, Lithuania, Luxembourg
Other (N=1)	Germany

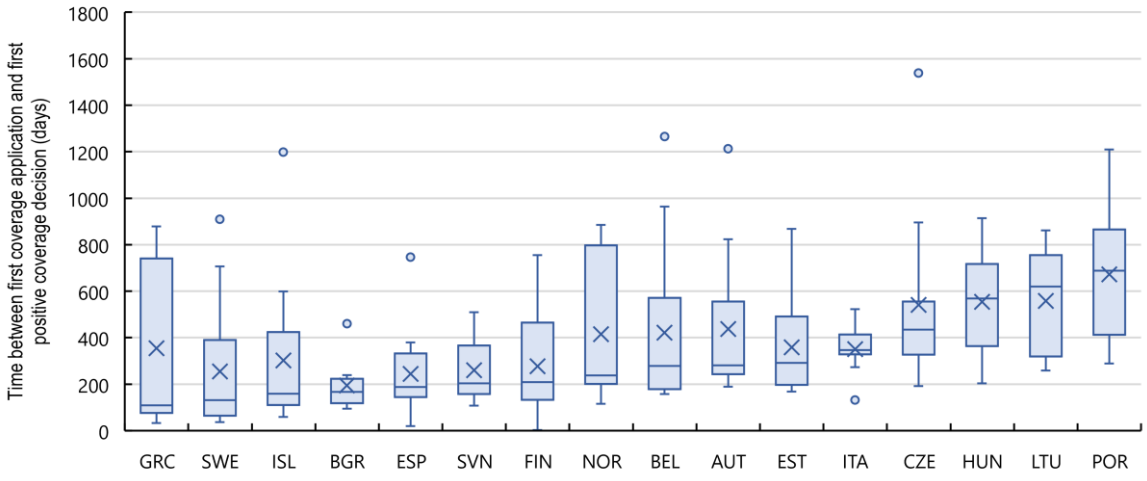
Note: Greece: HTA procedure only introduced in 2018, when the HTA and Reimbursement Committee was established by law. Germany: All products with a central marketing authorisation are, by default, covered by sickness funds. However, a systematic and formal assessment of the "added therapeutic benefit" of new medicines is imposed to negotiate the price according to the therapeutic value of a drug with effect 6 months/from the 7th month after market launch (new legislation in 2022). Lithuania: HTA process only introduced in 2020. Sweden: Regions make decisions for pharmaceuticals that are for inpatient care. There are no definite decisions made regarding coverage and pricing. Slovenia: There is no HTA agency. The economic part (HTA) dosser of the company is evaluated at the Health Insurance Institute together with the clinical part of the application. The Reimbursement Committee, the independent body under the Health Insurance Institute, consisted of external experts, assess the applicable and prepare the reports, that are publicly available.
Source: OECD survey on access to novel medicines 2021.

56. With the exception of Bulgaria and Greece, the total time between first coverage application to first *positive* coverage decision accounted for the largest share of time between marketing authorisation and coverage decision[20]. For half of responding countries this process took between a median of six months to one year. However, it took less than six months in Greece, Sweden, Iceland, and Bulgaria, and more than 12 months in the Czech Republic, Hungary, Lithuania, and Portugal. It is not surprising that this time difference generally represented the largest share of time from marketing authorisation to positive coverage decision given that it is influenced by several factors. For those product/indication pairs with a successful coverage decision on the first attempt, this includes the nature and performance of pricing and coverage-decision making processes in the country. However, it is important to recognise that the performance or pace of pricing or coverage decision-making processes cannot be interpreted from these data, as clock stops have not been considered. In other cases, this time difference may also reflect delays related to one or multiple submissions, whereby unsuccessful negotiation(s) failed on the first or subsequent attempts (see Section 2.2.2). Furthermore, in contrast to other responding countries, in both Greece and Bulgaria time to first application (Figure 2.9) accounted for a much larger share of the total time to positive coverage decision than the coverage process itself.

[20] However, it is important to note that the share of each time period as a proportion of the total time between marketing authorisation and positive coverage decision also differed substantially according to the medicine.

Figure 2.9. Time between first coverage application and first positive coverage decision, in days (Period 3)

For half of responding countries, the time between first coverage application and first positive coverage decision ranged from six months to a year and a half



	GRC	SWE	ISL	BGR	ESP	SVN	FIN	NOR	BEL	AUT	EST	ITA	CZE	HUN	LTU	POR
No. covered	9	14	12	9	14	13	15	13	13	13	9	13	12	7	7	12
Available dates	9	12	11	8	13	13	12	11	13	12	8	12	11	7	7	12
- No. with EAS	5	1	1	1	7	3	0	1	9	1	3	5	3	5	0	6

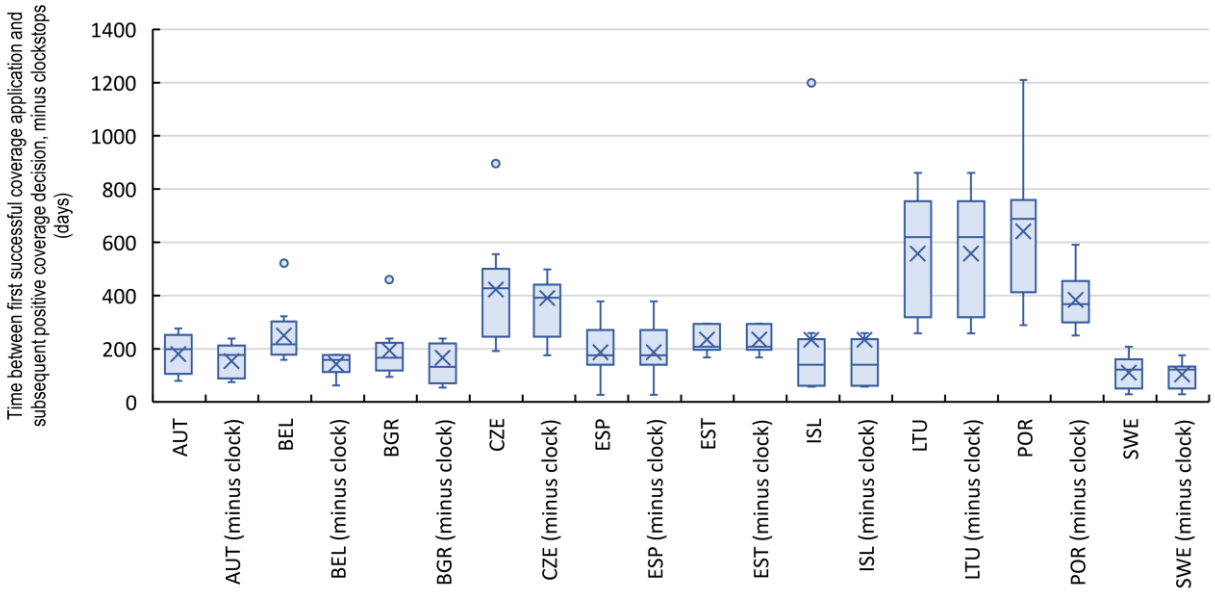
Note: X = average time in days per country, across the count of product/indication pairs; EAS = early access scheme, either named-patient or population-based (see Box 2.2, and Table AE.3 in Annex E)
Based on *covered* products with available date information, from a non-representative convenience sample of 15 product/indication pairs. The product/indication pairs for which these time periods are computed differs among countries.
Source: OECD survey on access to novel medicines 2021.

57. **Clock stops[21] should be considered when interpreting the time between applying for and granting of coverage as a measure of the nature and performance of coverage decision-making processes.** Without considering clock stops, the process from first successful coverage application to first positive coverage decision, took between six to twelve months in more than half of responding countries (see Figure AE.11, Annex E). However, available data allowed a deeper analysis for a subset of countries (Figure 2.10). Several countries mentioned that there was no clock stop for any of the production/indication pairs (Spain, Estonia, Iceland, Italy, and Lithuania) or only for a few of the sample products (Sweden). Portugal, however, had the longest median clock stop over the sample with available data, at more than eight months, followed by Belgium at around four months (Figure AE.12, Annex E). Clock stops also varied by medicine (Figure AE.13, Annex E). Accounting for clock stops (i.e. taking the clock stop duration out of the time period calculation), the median time between first successful coverage application and positive coverage decision dropped significantly for Portugal and Belgium, from almost two years to one year, and around seven to five months, respectively (Figure 2.10). Country order from lowest to highest median time difference also changed slightly. This effect is likely to be much greater with a larger sample.

[21] Clock stops refer to any period during which the evaluation of a medicine is officially stopped, for example while awaiting submission of additional information or while negotiations are underway.

Figure 2.10. Time between first successful coverage application and subsequent positive coverage decision, minus clock stops, in days (Period 3b)

The time between first successful coverage application and subsequent positive coverage decision changed significantly for some countries when clock stops were taken into account



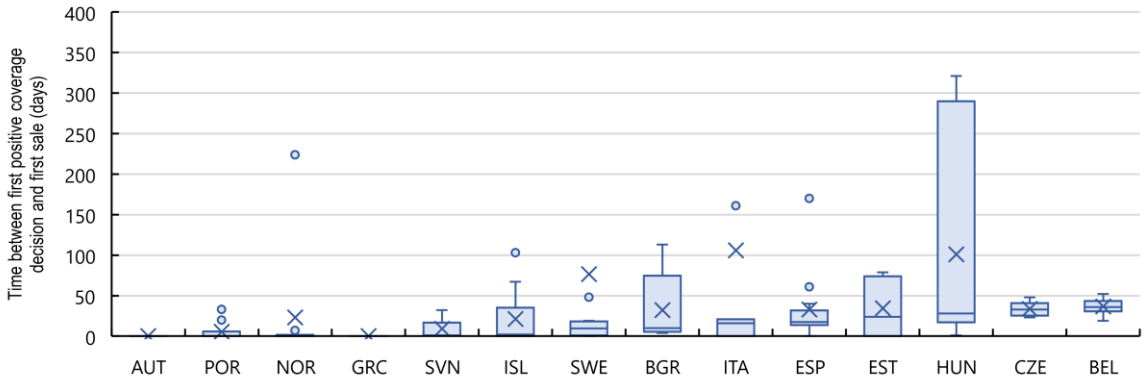
No. covered	*13*	*13*	*9*	*12*	*14*	*9*	*12*	*7*	*12*	*14*
Available dates	*12*	*11*	*8*	*11*	*11*	*7*	*11*	*7*	*12*	*12*
- No. with EAS	*1*	*8*	*1*	*3*	*6*	*2*	*1*	*0*	*6*	*1*

Note: "Minus clock" means that the clock stop duration has been taken out of (i.e. subtracted from) the estimate; X = average time in days per country, across the count of product/indication pairs. EAS = early access scheme, either named-patient or population-based (see Box 2.2, and Table AE.3 in Annex E). Hungary and Italy were removed as data were only available for one and three product/indication pairs, respectively. Based on *covered* products with available date information, from a non-representative convenience sample of 15 product/indication pairs. The product/indication pairs for which these time periods are computed differs among countries.
Source: OECD survey on access to novel medicines 2021.

58. The date of first (reimbursed) sale occurred around one month or less after the positive coverage decision in most responding countries (Figure 2.11). Several countries provided first sales dates prior to granting of coverage, likely reflecting access on an individual patient basis such as through named-patient early access schemes. However, in many cases this would be considered as "pseudo" access as the product may only be accessible for a limited number of patients and not necessarily widely accessible to all patients through publicly funded coverage. In these cases, the sales dates were adjusted to the positive coverage decision dates. This issue is further discussed in the following section.

Figure 2.11. Time to first sale after positive coverage decision, in days (Period 4)

First sale occurred around one month or less after the positive coverage decision in most responding countries



	AUT	POR	NOR	GRC	SVN	ISL	SWE	BGR	ITA	ESP	EST	HUN	CZE	BEL
No. covered	13	12	13	9	13	12	14	9	13	14	9	7	12	13
Available dates	12	10	10	9	12	11	12	8	12	14	8	7	9	13
- No. with EAS	1	5	1	5	3	1	1	1	5	8	3	5	3	9

Note: X = average time in days per country, across the count of product/indication pairs; EAS = early access scheme, either named-patient or population-based (see Box 2.2, and Table AE.3 in Annex E). Outliers not shown: Italy 1008 days; Sweden 796 days. If first sales date appeared before coverage decision, first sales date was assumed to be the same as the coverage decision date.
Based on *covered* products with available date information, from a non-representative convenience sample of 15 product/indication pairs. The product/indication pairs for which these time periods are computed differs among countries. The time difference calculations do not account for population-wide early access schemes that may be used to accelerate access in some countries.
Source: OECD survey on access to novel medicines 2021.

59. Due to a lack of data availability, it was not possible to undertake an in-depth sub-analysis on time differences for those products for which coverage was denied, the decision did not proceed, or the HTA and/or coverage decision was in process. However, from the few data points that were available, it appears that time between marketing authorisation and first application for these medicines would be considered outliers in most countries compared to the estimates shown in Figure 2.8. The median time to first application was more than a year in Malta, based on a sample of seven product/indication pairs in the review process as at 01 October 2021. It is common for Malta to receive reimbursements later than larger markets. However, if there is a clinical need and the company has not applied for a medicine to be included on the Government Formulary List, there is flexibility allowing Clinical Consultants and Specialists to request that new pharmaceuticals be introduced.

2.2.2. The feasibility of producing decomposed time-to-access metrics routinely and at scale is hampered by the current data landscape

60. **Collecting and analysing time differences between the sequences of events in the lifecycle of a medicine present their own unique challenges to routine data collection, particularly if required at scale.** Existing measures of time-to-access generally require collection of only two main dates for each product/indication pair: marketing authorisation and granting of coverage (or inclusion of a product in positive reimbursement list). While gathering these data may be considered fairly feasible, it does not provide insight into access bottlenecks in countries, and decomposition of time periods based on the sequences of events in the lifecycle of a medicine are more desirable. Consequently, this survey collected retrospective date data for three different stages: HTA; coverage; and sales (see Table AD.2, Annex D, for a list of survey questions, and Table AE.7, Annex E for an overview of date data provided by countries). **Detailed process-related date data are generally not available in the public domain, and challenging to obtain even by countries themselves, especially at the level of the medicine's indication**.

Feasibility of date gathering across these stages largely depends on the number of different institutions involved, which depends on within-country processes and the interoperability of any internal databases used to aid data collection. This exercise is further complicated in those countries with decentralised evaluation processes, which may be a particular issue for inpatient medicines. Despite these challenges, most responding countries were able to provide data points across these stages for most of their respective covered index products (see Table AE.7, Annex E). Cyprus and Luxembourg did not report any date information; this particular analysis was not applicable to Malta in which none of the product/indication pairs were covered.

61. Even if decomposed data can be obtained, **analysis and interpretation is challenged by differences in the sequences of events / processes**. The sequence of HTA, coverage application, and decision processes are not the same in every country, nor for every product/indication within one country. For example, some responding countries allow companies to submit applications for HTA and/or coverage prior to EU marketing authorisation (e.g. Belgium – under certain conditions; Estonia – e.g. on submission by a medical association; France; and Norway – if a company is able to provide the dossier). In others, e.g. Lithuania, application for coverage is not possible before marketing authorisation. In Spain, a company may communicate its intent to commercialise a product before the marketing authorisation date (only for informative purposes and in order to get the therapeutic positioning report elaboration process started), but an HTA dossier cannot be submitted to the pricing and reimbursement authority until after marketing authorisation has been granted. As previously mentioned, HTA and coverage applications are filed simultaneously in most EU Member States (Table 2.2). Interpretation of results also needs to consider that some stages are not applicable to some countries (e.g. coverage in Germany; HTA in Lithuania – see Table AE.6, Annex E). When computing the delays in different parts of the process, "negative durations'' also needed to be taken into account, when part of the process had taken place earlier than expected (e.g. HTA or coverage application before marketing authorisation). Several countries also allow sales before granting of coverage (discussed below). While the analyses shown in this paper used the defined time periods as described in Figure AE.9, Annex E, this exercise would be more complex if considering further data such as on early access coverage schemes or health technology assessment processes.

62. **Decomposed time-to-access metrics are affected by the presence of multiple submissions** for one product in the same indication, but were not accounted for in this exercise. This is a particular problem in the case where a product is initially denied coverage or the application is withdrawn, and then granted coverage after a subsequent application. While it is not necessarily possible to discern this information from the OECD survey, responses from some countries pointed to this (e.g. in Belgium, there was no reimbursement decision on the first file for three products because the company withdrew their application; in Austria one product was delisted from the code of reimbursement and the company applied again). Without knowing this additional information, it is challenging to interpret decomposed time-to-access metrics about the nature and performance of country decision-making processes. However, feasibility of collecting such detailed information is limited by the lack of availability of data which is almost certainly not in the public domain. This becomes even more challenging if the products are approved in more than one indication.

63. **Clock stops**[21] **must be considered if interpreting time between applying for and granting of coverage as a measure of the nature and performance of coverage decision-making processes in each country, but may not be tracked routinely**. Most responding countries were able to provide an indication of the clock stop time between the first successful application and granting of coverage for their respective covered product/indication pairs, although accurate date information may not be publicly available – see Table AE.7, Annex E. Some countries gave an indication that a clock stop occurred but may not have specified the specific number of days for all products (e.g. Belgium, Hungary, Italy, Slovenia). In others, the legal framework does not allow for clock stops (e.g. Iceland). A few countries were also able to provide specific reasons behind the clock stop (e.g. Austria, Belgium, Czech Republic, Estonia, Portugal), for example: determination of reimbursement eligibility; awaiting submission of missing

information or further evidence from the company; managed entry agreement negotiations; price negotiations; and awaiting legal time to comments etc. Clock stop data are not necessarily routinely tracked within current data systems and may require significant administrative burden to identify. In Italy, for example, the current system does not track clock stops but the new one intends to. Some countries, however, such as Portugal, have electronic submissions that record each clock stop and are able to disaggregate timing by reasoning (e.g. submission of evidence required by the company, negotiation process etc).

64. **The date of first sale may not be an adequate proxy for date of population access or product "launch"**[5], particularly in those countries in which sales may occur prior to the positive coverage decision on a named-patient basis. Alternative access mechanisms in some countries may allow for a product to be sold (and even reimbursed) prior to marketing authorisation or coverage (Box 2.1, Box 2.2), so date of first sale does not necessarily reflect general population access (unless early access is provided via population-based schemes). In Austria, for example, first sales date can be prior to the application submission date, since in justified individual cases prescribing through the social security system is possible even if no formal evaluation and final decision on reimbursement has been made (i.e. for products outside of the positive reimbursement list). In Estonia, sales prior to coverage may be possible if funded by patients or treatment support institutions. In Finland, a product can be sold prior to the coverage decision if it is available for marketing, or used in a hospital setting if needed. Italy has a specific process for which the negotiation procedure has started but sales without national health service reimbursement is possible. Using first sales date can have a large effect on time-to-access metrics: for one product first sales date was more than three years prior to the positive coverage decision. Furthermore, utilisation data may not be able to distinguish reimbursed versus non-reimbursed sales and is also only possible at the level of the product and not indication (see Section 4.). Perhaps a better metric might be to consider first sales date after granting of coverage, or to remove the metric of "first sales" altogether, and only consider granting of coverage or inclusion in a positive list as a proxy for patient access. In this paper, if the date of first sales provided occurred prior to the positive coverage decision, the sales date was modified to be the same date as the coverage decision. While not explicitly analysed in this study, consideration of the impact of population-wide early access coverage schemes, such as those used in France, warrants further exploration.

65. **The feasibility of producing decomposed time-to-access metrics routinely and at scale is hampered by the current data landscape and the administrative burden for countries in gathering information pertaining to different stages in the lifecycle of a medicine.** This was a challenging exercise in data collection, as well as interpretation, for a small sample size of only 15 product/indication pairs. Some country (internal) data systems may aid analysis – for example, Belgium and Portugal can track the progress of these processes over time in a centralised database. Further work should focus on the specific time periods of most interest to policy makers, and examine the readiness of country data systems to provide this information routinely. Existing collaborative platforms such as EURIPID could potentially be used to produce proxy analyses on time from marketing authorisation to reimbursement. The database contains product-level time series information on coverage status of (mostly outpatient) medicines and can provide an approximate start date of reimbursement for a product within a country. A simple comparison between the OECD survey data on coverage decision date and EURIPID reimbursement data found a median deviation of around one month between the two data sources. However, this estimate would only be relevant for the first indication of a product, and does not consider any of the abovementioned issues regarding decomposition of time periods.

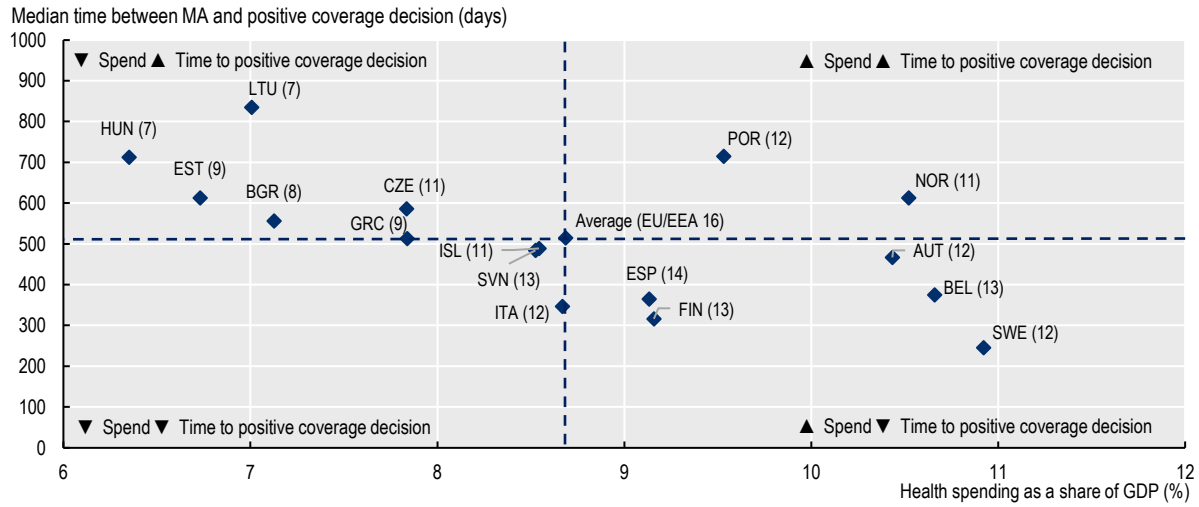
2.3. Time-to-access differences may be associated with economic factors in countries

66. As noted in the literature, time-to-access differences may be associated with the economic situation in countries. To explore this idea further, it is possible to compute median (or average) time differences against a measure of spending, such as health spending as a proportion of Gross Domestic Product (GDP). Figure 2.12 shows this relationship using two time periods as examples: median time between marketing authorisation and positive coverage decision, excluding early access coverage schemes (panel A), and median time between marketing authorisation and first application for HTA and/or coverage (panel B). Both graphs display the relationship across the total medicine sample, with time differences calculated for a different number of product/indication pairs in each country.

67. Countries may fall within one of four quadrants in Figure 2.12: upper left – lower spending / longer time; upper right – higher spending / longer time; lower left – lower spending / shorter time; and lower right – high spending / shorter time. The centre of the quadrant charts is the average across the data points used in the respective samples. As an artefact of the small sample size of heterogenous medicines, the quadrant within which some countries fall in each chart may change according to the sample and metric used (e.g. average versus median, similarly to the issues already highlighted in Box 2.3). Nevertheless, Figure 2.12 suggests that, in general, while countries with lower health spending have a longer time from marketing authorisation to positive coverage decision, they also wait longer to receive an application by companies. The relationship between time-to-access differences according to different time periods, relative to a measure of health spending, is a metric that warrants further exploration with more representative data.

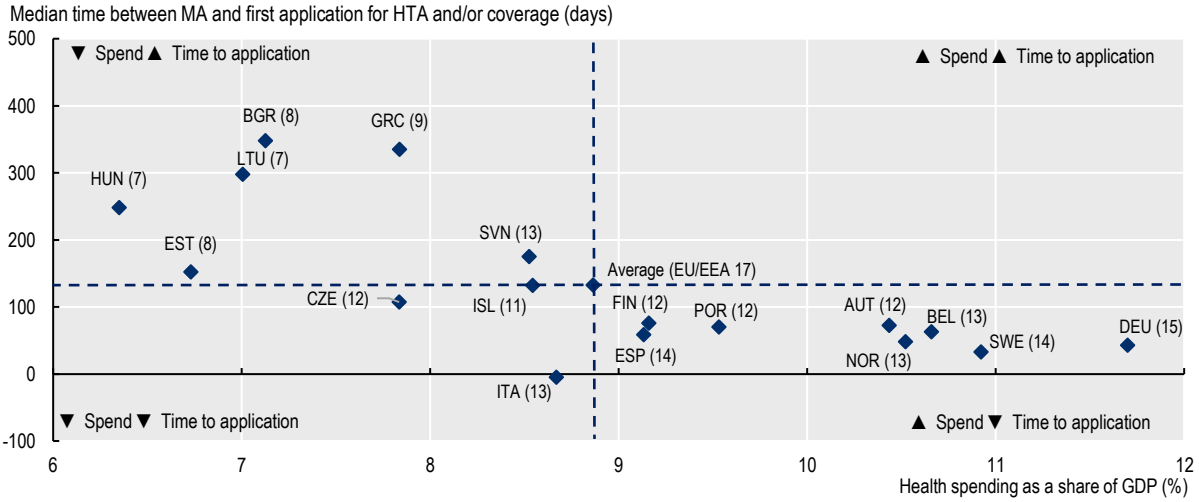
Figure 2.12. Median time differences (excluding early access coverage schemes) relative to health spending as a proportion of GDP

Panel A: Median time between MA and positive coverage decision, relative to spending (n=16)



	AUT	BEL	BGR	CZE	ESP	EST	FIN	GRC	HUN	ISL	ITA	LTU	NOR	POR	SVN	SWE
No. covered	13	13	9	12	14	9	15	9	7	12	13	7	13	12	13	14
Available dates	12	13	8	11	14	9	13	9	7	11	12	7	11	12	13	12
- No. with EAS	1	9	1	3	8	3	0	5	5	1	5	0	1	6	3	1

Panel B: Median time between MA and first application for HTA and/or coverage, relative to spending (n=17)



	AUT	BEL	BGR	CZE	DEU	ESP	EST	FIN	GRC	HUN	ISL	ITA	LTU	NOR	POR	SVN	SWE
No. covered	13	13	9	12	15	14	9	15	9	7	12	13	7	13	12	13	14
Available dates	12	13	8	12	15	14	8	12	9	7	11	13	7	13	12	13	14
- No. with EAS	1	9	1	4	0	8	3	0	5	5	1	5	0	1	6	3	2

Note: EAS early access scheme, either named-patient or population-based (see Box 2.2 and Table AE.3, Annex E). Based on *covered* products with available date information, from a non-representative convenience sample of 15 product/indication pairs. Brackets denote the number of product/indication pairs for which the time differences were computed. The time difference calculations do not account for population-wide early access schemes that may be used to accelerate access in some countries, meaning the time difference displayed could be shorter for some countries. Median time differences relative to a measure of health spending may also change according to the sample and metric used.
Source: OECD survey on access to novel medicines 2021; OECD/European Observatory on Health Systems and Policies (2021[25]), health spending data refer to 2019.

3. Affordability dimension: measures were confounded by a lack of transparency

68. This section explores some indicators of affordability, using (non-representative) data from the OECD survey and EURIPID database. Section 3.1 examines affordability to the system, looking at annual treatment cost relative to a parameter of wealth for a subset of *covered* index product/indication pairs. Section 3.2 looks at the types and levels of cost-sharing for the set of sample product/indication pairs. The utility and feasibility of collecting and interpreting these affordability indicators are discussed throughout. Annex F presents additional details on methodology not included in the body of this paper.

3.1. Current estimates of affordability to the health system are challenging to elicit and difficult to interpret

3.1.1. System-level affordability indicators were confounded by the existence of confidential rebates and discounts, and cross-country variations in levels of consumption and health expenditure

69. One option to compare the relative affordability of medicines to the system is to estimate the ratio of costs of treatment in a country relative to a measure of national wealth. GDP per capita, for example, can be used as a proxy for wealth in countries, and medicine prices can approximate costs of treatment. However, pharmaceutical price comparisons are very complex. Previous literature highlights the need to consider many different aspects, including the type of price comparison, the price type, medicine selection, data sources, units of analyses, exchange rate, and country weighting (Vogler, Schneider and Zimmerman, 2017[31]). Unlike other indicators, aggregating medicine prices is not appropriate. In general, price comparisons should only be made for individual medicines on a "like-for-like" basis, with more complex methods required for any aggregate analyses (Vogler et al., 2021[32]; World Health Organization and Health Action International, 2008[33]; Habl et al., 2018[34]; The Dental and Pharmaceutical Benefits Agency (Sweden), 2020[35]; Vogler, Schneider and Zimmerman, 2017[31])

70. The panels in Figures 3.1 and Figure AF.1, Annex F, show the variations in relative affordability to the system, based on ex-factory prices, for thirteen of the index product/indication pairs (subset chosen due to missing data). The annual treatment cost for each medicine was estimated using the treatment regimen in Table AF.1, Annex F and expressed relative to GDP per capita. See Annex F, for more details on methodology.

71. For this particular subset of product/indication pairs, *relative affordability* appeared to vary significantly between countries and medicines. The cost of one year's treatment far exceeded the GDP per capita in some cases. In eight out of thirteen product/indication pairs, Bulgaria appeared to have the lowest relative affordability among the responding countries. Country variations in medicine price and affordability have been explored elsewhere in the literature (e.g. (Cuomo, Seidman and Mackey, 2017[36]; Moye-Holz and Vogler, 2021[37]; World Health Organization, 2018[38])).

72. It is important to note that the relative affordability **estimates did not take into account the existence of or impact of confidential discounts or managed entry agreements**. The existence of confidential agreements or discounts in the sample was high – more than 70% of the total sample of country-product/indication pairs (with information on ex-factory prices) mentioned the existence of a confidential agreement or rebate. The proportion was similar across sample products, each having a confidential discount or rebate in over half of the responding countries.

73. The panels presented in Figures 3.1 and Figure AF.1, Annex F, offer some insight into the affordability of specific products, however, no conclusions on the general affordability of medicines within countries should be drawn without additional evidence from more elaborate analyses. **Not only would such conclusions be biased by the choice of medicines in the sample and the existence of confidential discounts or rebates, but also by the proxies chosen to approximate costs of treatment and the wealth of the countries**. To estimate the total cost countries are bearing for a specific medicine, the price of a product would need to be multiplied by the consumption level (or eligible population), which varies greatly across countries and medicines. Since most countries provided incomplete consumption data, the individual medicine price was chosen as a proxy. Similarly, GDP per capita was used as a proxy for wealth, but other estimates such as health spending as a share of GDP per capita could be explored. The panels in Figures 3.1 and Figure AF.1, Annex F, therefore need to be understood as countries' ability to pay for specific products assuming similar levels of consumption and health expenditure.

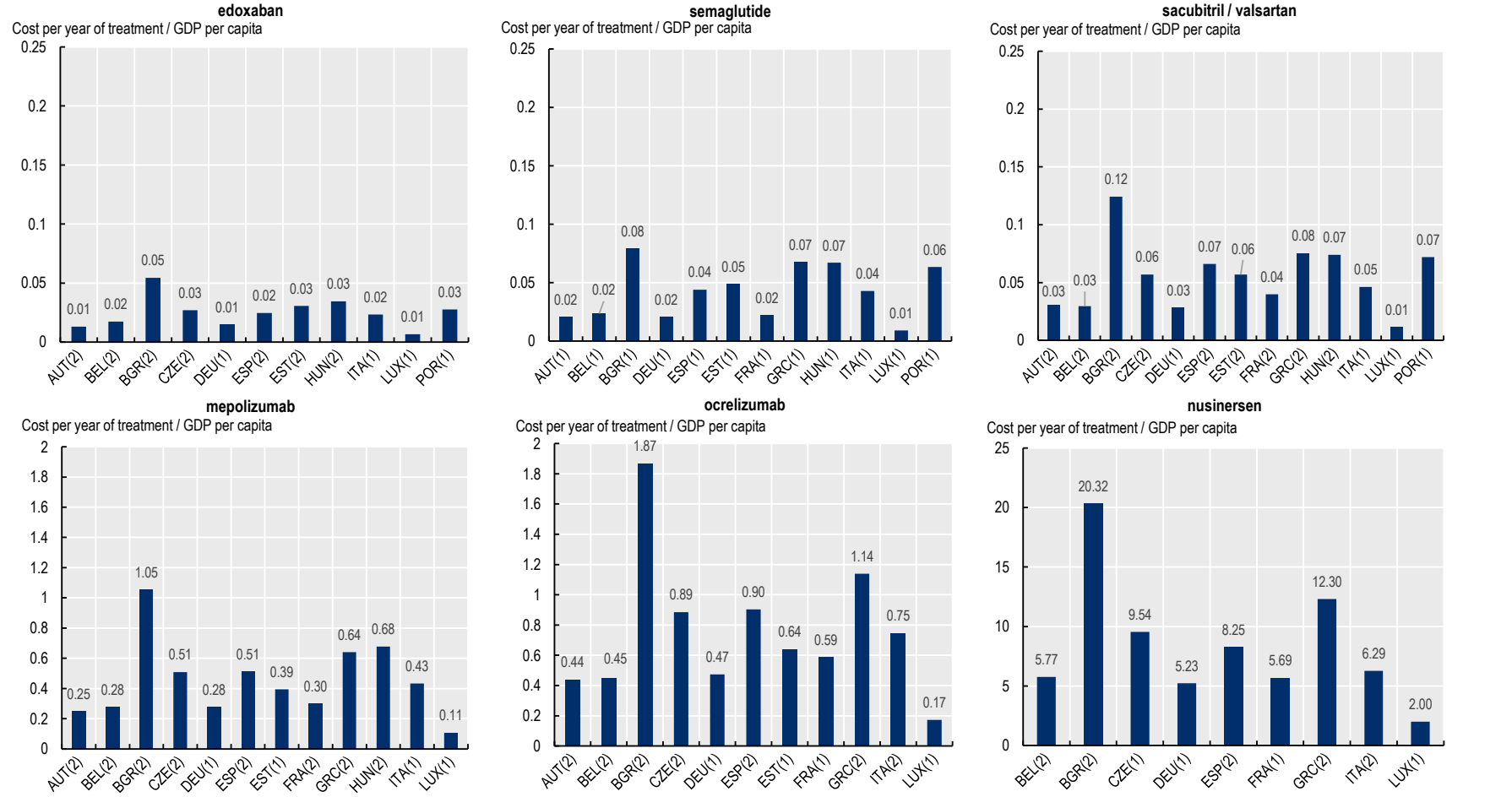
3.1.2. Meaningful affordability estimates are challenging to produce due to the lack of comparative data

74. In most European countries, official price data of publicly funded medicines are, at least in part, publicly accessible, although the price types disclosed may differ. Access to such information may be limited for the public, for example requiring subscription fees to access medicine price databases, and in other cases may be considered confidential (Vogler, 2022[39]). As outlined above, the high presence of confidential discounts and rebates reduces the meaningfulness of price comparisons made using official price data. Nevertheless, of 21 countries that participated in this study, fourteen were able to provide ex-factory prices for covered products. Some countries provided wholesale prices (e.g. Finland, Iceland, Norway, Slovenia, Sweden); for comparability reasons these were excluded in the presented analysis. The need to obtain comparative information at a very detailed level (e.g. ex-factory price for a reimbursed product with a specific strength, and similar pharmaceutical form and pack size) limited the number of datapoints that could be included in the analysis and ultimately resulted in the use of a considerably smaller sample size than initially foreseen. The literature on price comparisons suggests that comparisons should only be made on a "like-for-like basis", precluding price data from countries which had not authorised the exact or similar presentation requested by the survey. These exclusion criteria effectively resulted in the inclusion of only 131 datapoints out of the 231 covered medicine-country combinations.

75. Existing international price databases can be leveraged as an alternative to survey data. As mentioned in Section 1.2.3, medicine price data for 26 EU countries is already collected and maintained in the European price database, EURIPID. The database contains data on official prices of publicly reimbursed medicines, predominantly in the outpatient setting, that are published by public authorities in line with the EC Transparency Directive (Council Directive 89/105/EEC 89\105\EC). Although the EURIPID database is mostly limited to medicines administered in the outpatient sector, it was able to provide medicine price data for more than 70% of medicine-country combinations collected by the survey. In addition, the database contains further product-level information on coverage status and the existence of managed entry agreements.

Figures 3.1. Estimated cost per year of treatment relative to GDP per capita, using ex-factory prices, at 01 October 2021

Affordability estimates based on ex-factory prices are of limited meaning without considering confidential discounts and rebates, consumption, and health expenditure



Note: Example of how to read the graph: An annual treatment with mepolizumab would be an estimated 1.05 times the GDP per capita in Bulgaria. Based on *covered* products with available ex-factory price information, from a non-representative convenience sample of 15 product/indication pairs in 21 responding countries. See Figure AF.1, Annex F, for the remaining graphs. Scales differ by medicine.
Source: (1) OECD survey on access to novel medicines 2021; (2) EURIPID database, 2021.

3.2. Patient-level affordability measures are difficult to estimate and require an in-depth understanding of cost-sharing mechanisms

3.2.1. Cost-sharing mechanisms have an important impact on the financial burden carried by patients

76. Like the previous indicator, the affordability of medicines to patients is best estimated for specific products, and not at the aggregate level (see section 3.1.1). One option to identify the affordability of medicines for patients includes taking the ratio of the out-of-pocket costs and the patients' ability to pay. A measure of wage (e.g. average wage) can be used as a proxy for patients' ability to pay.

77. The panels in Figure 3.2 below and Figure AF.2 in Annex F, show variations in the affordability for patients[22] for thirteen of the index product/indication pairs (subset chosen due to missing data). Data on out-of-pocket costs come in different forms, which reflects the various types of cost-sharing used in countries and presented a challenge for data analysis and presentation. For example, for product/indication pairs covered through coinsurance, some countries provided out-of-pocket costs as a percentage of the retail or reimbursement price. Nominal out-of-pocket costs needed to be calculated ex-post, including attempting to account for any additional information on caps. The panels in Figure 3.2 and Figure AF.2, Annex F, group countries by type of cost-sharing mechanism to facilitate interpretation. Affordability for the patients was expressed as the number of days of average wages needed to pay for one month of treatment, assuming that the patient had not received any other medicines nor reached an annual cap[23].

78. For this particular subset of product/indication pairs, the financial burden for the same product varied significantly from country to country. Patients seemed to bear the highest financial burden where patient contributions were structured as coinsurance amounts, which aligns with the findings of previous OECD work (Chapman, Paris and Lopert, 2020[14]). However, no general conclusions should be drawn from this product-level analysis, as type and level of cost-sharing not only varied across countries (Figure 3.3) but also across medicines (Figure 3.4). This was particularly relevant for those medicines administered in hospital settings, which were often free of charge for the patient. It is therefore likely that the sample is misrepresenting the most prominent type of cost-sharing used within countries, and leading to biased conclusions on the financial burden for patients. Types and levels of cost-sharing may also vary depending on population segments, which was not considered in this particular analysis.

3.2.2. Some features of cost-sharing mechanisms are complex and country-specific making comparisons between countries challenging

79. The estimates presented here assume that patients did not receive any other treatment, which limits its utility. Seven of the 21 responding countries declared annual ceilings on out-of-pocket costs which might be reached quicker by patients receiving multiple treatments, perhaps causing an underestimation of the affordability for certain populations. This issue was partially addressed by presenting the affordability of a month of treatment.

80. Some features of cost-sharing mechanisms are country-specific and difficult to quantify, which led to their exclusion, yet hampers the meaningfulness of the analysis. Countries put in place various measures to enhance financial protection for patients, through different caps on spending as well as

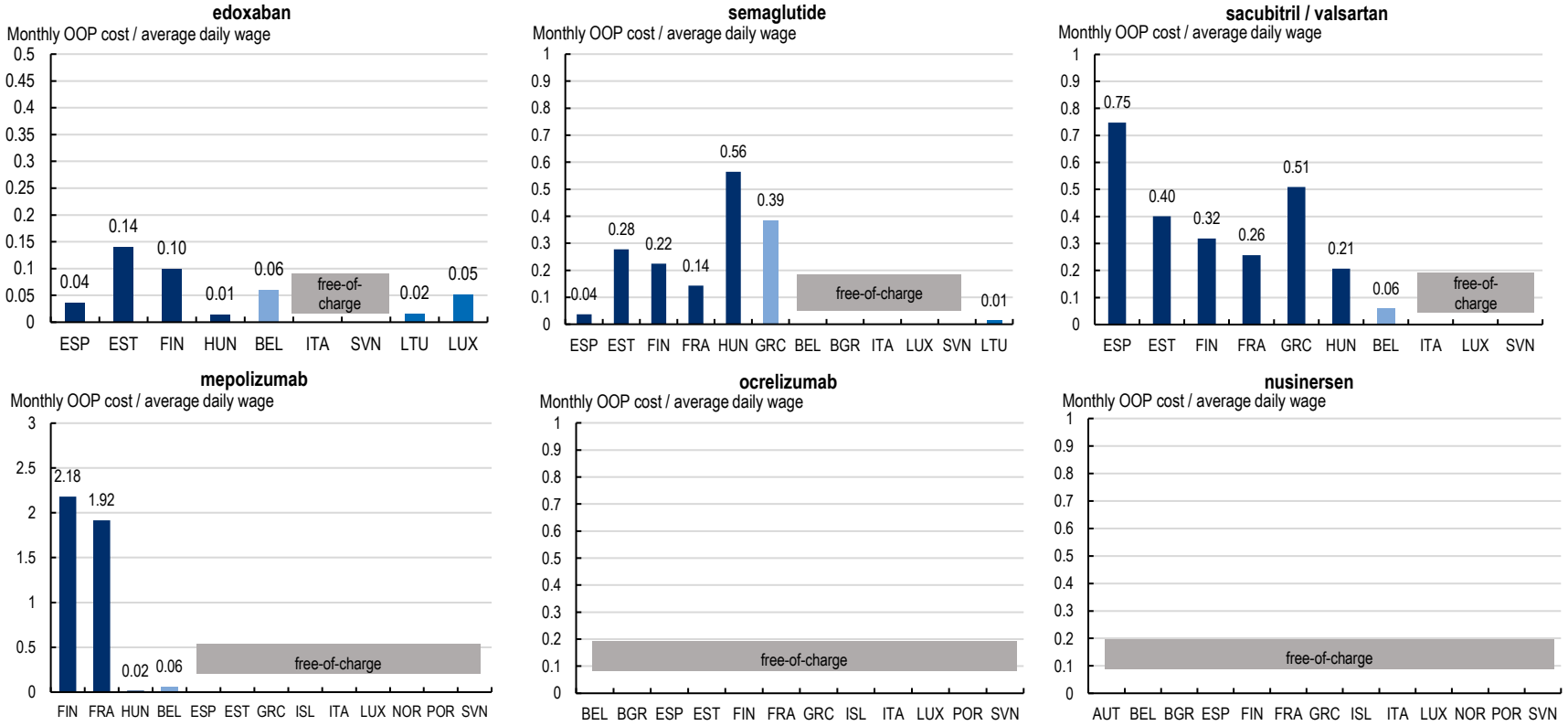
[22] Here, cost-sharing arrangements refer to an adult patient who was not entitled to any special concession or exemption from cost-sharing at the time of data collection

[23] Except in the case of Finland, where a patient would reach the annual cap with one month's treatment of several of the product/indication pairs. In this case, out-of-pocket costs were adjusted to reflect this annual cap.

differences in reimbursement levels for various population segments. Some examples of such country-specific features include criteria-based caps (e.g. Belgium where the cap depends on the patient's income and other social factors), criteria-based coinsurance percentages (e.g. Estonia where children under 4 and children between 4 and 16 profit from a higher reimbursement rate than adults), and complex coinsurance models (e.g. Germany where patients contribute through a 10% co-payment rate, with a minimum of 5 EUR and maximum of 10 EUR per prescription). Out of seven countries that described an annual cap, only Finland's was taken into account in this analysis as it did not depend on any additional criteria and was directly applicable to a month's worth of treatment. The complexity of cost-sharing mechanisms in European countries has been extensively described by Vogler et al. (2018[26]) and (Thomson, Cylus and Evetovits, 2019[40]).

Figure 3.2. Estimated out-of-pocket costs for one month of treatment relative to average daily wage, at 01 October 2021

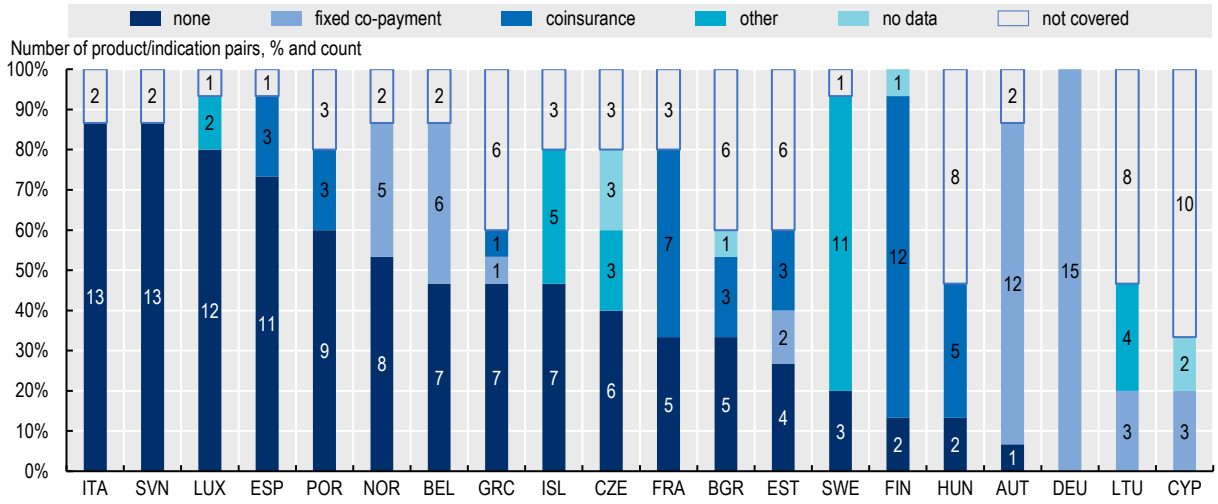
Financial burden for the patient differed by country and medicine, and depended on the type and level of cost-sharing



Note: OOP (out-of-pocket) costs. Columns are color-coded by type of cost-sharing: coinsurance, fixed co-payment, other (e.g. deductible, extra-billing). Example of how to read the graph: purchasing one month of treatment with mepolizumab would cost around 2 day's wages in Finland and France, whereby patient contributions are structured as coinsurance.
Based on *covered* products with available out-of-pocket cost information, from a non-representative convenience sample of 15 product/indication pairs in 21 responding countries. Finnish estimates were adjusted based on the annual cap amount, where a patient would reach this cap with one month's treatment. See Figure AF.2, Annex F, for the remaining graphs. Scales differ by medicine.
Source: OECD survey on access to novel medicines 2021.

Figure 3.3. Proportion of sample product/indication pairs by types and levels of cost-sharing across countries

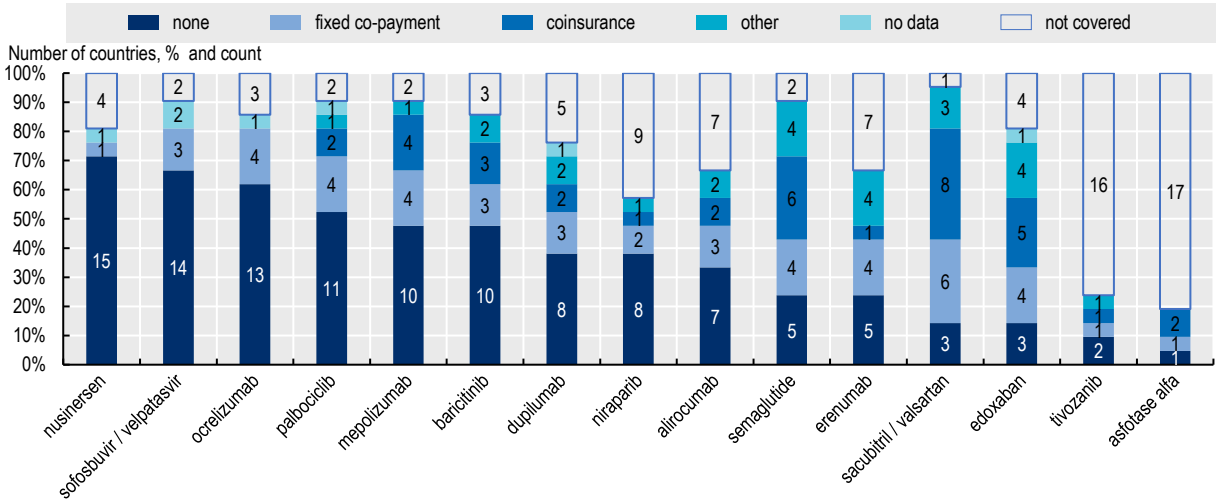
The types and levels of cost-sharing varied across countries



Note: None = none, free of charge. Proportions based on index product/indication pairs that were covered across countries, as at 01 October 2021. Maximum number of covered product/indication pairs per country was 15. Data labels show counts of product/indication pairs in each category, per country. In Germany, patients are generally required to contribute to the costs of pharmaceuticals through a 10% co-payment rate (with a minimum of EUR 5 and a maximum of EUR 10 per prescription). Malta was excluded as no product/indication pairs were covered.
Source: OECD survey on access to novel medicines 2021.

Figure 3.4. Proportion of countries by types and levels of cost-sharing across product/indication pairs

The types and levels of cost-sharing also varied across medicines



Note: None = none, free of charge. Proportions based on index product/indication pairs that were covered across countries, as at 01 October 2021. Maximum number of countries per product/indication pair was 21. Data labels show counts of countries in each category, per product/indication pair.
Source: OECD survey on access to novel medicines 2021.

4. Accessibility dimension: measures were affected by data limitations

81. This section explores some indicators of accessibility, using data from the OECD survey as well as the EURIPID database. Section 4.1 explores some of the challenges in interpreting cross-sectional data on consumption and approximate patient numbers. This is followed by some examples of time-series data that can be used to show delays in decision-making and uptake. Section 4.2 describes some of the overarching challenges with identifying comprehensive consumption data to inform metrics on patient accessibility. Annex G presents additional information and analyses not included in the body of this paper.

4.1. Measures of uptake provide insights into patient accessibility, but comparisons are limited by significant data gaps and confounders

82. **Estimates of availability of medicines, as measured by coverage status, cannot offer insight into patient access without considering data on actual use**. A medicine may be available (i.e. included in a list of covered products), and affordable, but not necessarily accessible to patients. To complement the previously discussed dimensions of availability and affordability (Sections 2. and 3. respectively), a combination of survey response and EURIPID data were used to compare the consumption of each *covered* sample medicine in each country (in milligrams and/or defined daily dose [DDD]) per 1000 population per day, estimated using consumption data covering the 12-month period prior to October 2021**.** Data included consumption of an active substance across all product presentations, regardless of pharmaceutical strength / form / pack size. Where data were available, consumption was compared using milligrams and defined daily dose[24], and supplemented with data on the approximate number of patients treated over the same time period. Data were not aggregated across products. The following sections outline some of the challenges faced with collecting and interpreting such data - see Annex G for further details.

4.1.1. Accessibility metrics cannot always be disaggregated to a sufficiently granular level to inform cross-country comparisons

83. **Utilisation (or consumption) measures cannot always be disaggregated to a sufficiently granular level to inform cross-country comparisons.** They are very challenging to develop at the product/indication-level as utilisation data generally reflect use across all approved indications of a product and should be considered in the context of the burden of disease and differences in clinical practice across countries (including the availability of alternatives). Consumption estimates presented here have limited interpretation and could not be meaningfully aggregated across the heterogenous sample of products.

[24] Milligrams is a preferred measurement unit to DDDs in some cases, for example: no WHO DDD exists for many active substances (e.g. in oncology whereby dosing is frequently based on body weight or body surface area); in certain cases DDD depends on the indication and consumption data cannot necessarily be disaggregated by indication; the DDD can change over time and changes may not be managed the same way in different countries; DDDs depend on the route of administration; and DDDs for combination products are on a unit basis. Some of the difficulties in gathering comparative data are outlined in Section 4.2

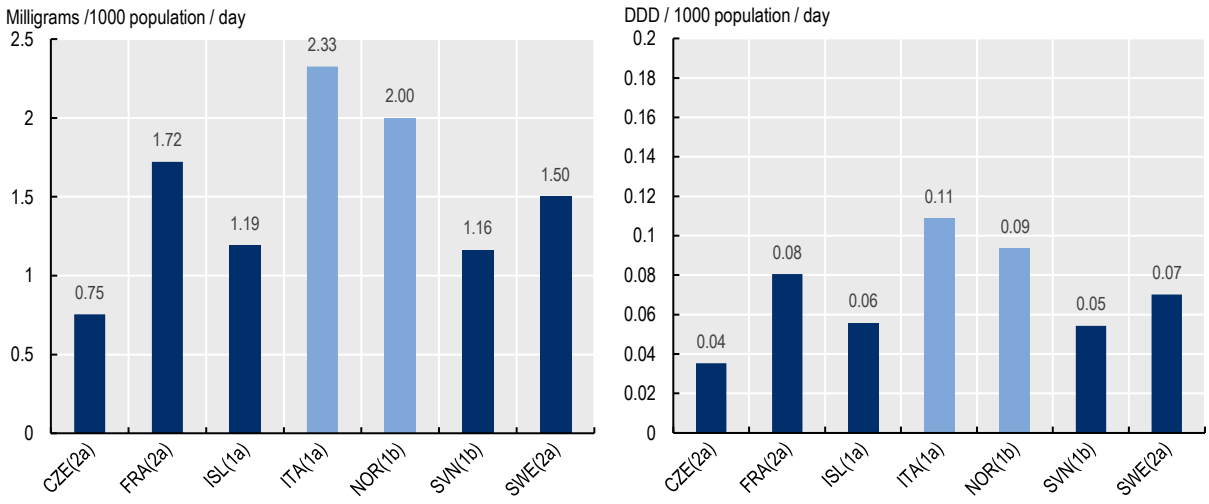
Nevertheless, this study was able to highlight some of the key challenges with collecting and interpreting utilisation data, particularly as they relate to characteristics of specific products.

84. Where data were available, the panels in Figures AG.1 and AG.2, Annex G, show consumption of each sample medicine in each country (in milligrams and/or defined daily dose [DDD]) per 1000 population per day. Large differences in consumption were seen across countries for each product; some countries had comparatively much lower consumption of some products than others, as expected, likely for several reasons that are discussed below. It is also important to note that, due to reporting delays, country data reflect estimates calculated using slightly different time periods. This can affect interpretation of the results since uptake also depends on the time elapsed since a positive coverage decision.

85. **Consumption data may be more readily comparable across countries for products administered in the outpatient setting, with a single indication, and with no or only limited available alternatives.** While none of the sample products precisely matched this criterion, *dupilumab* is presented as an example as there were no alternatives for severe atopic dermatitis at the time of initial marketing authorisation, and it was reported as being predominantly administered in the outpatient setting in most countries (Figure 4.1).

Figure 4.1 Consumption data may be more comparable for outpatient products with one primary indication, and no or limited alternatives

Example: *dupilumab*, predominantly administered in the outpatient setting, with no considered alternatives at the time of initial marketing authorisation



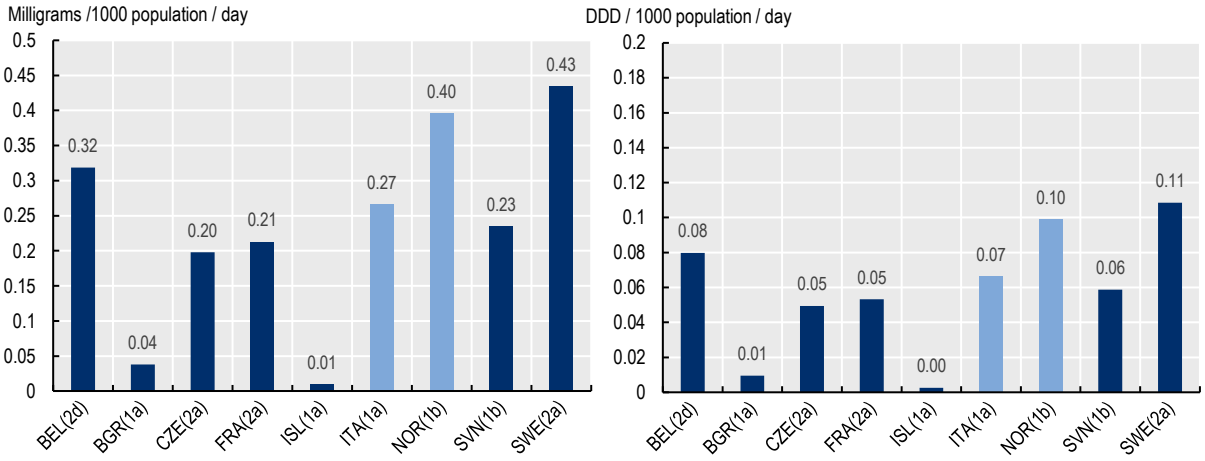
Note: most frequently administered in primary or ambulatory care; most frequently administered in the inpatient setting.
Estimated using total consumption over a yearly period: (a) 12 months prior to 01/10/2021; (b) 2021.
Source: (1) OECD survey on access to novel medicines; (2) EURIPID database.

86. In general, and as specifically pointed out by several survey respondents (Austria, Czech Republic, Estonia, France, Sweden), **consumption data at the level of the indication is not available, which negatively affects interpretation of any analyses**. This is most relevant for those products with more than one (main) approved indication, and for which some countries may not reimburse the product in all its approved indications. Those that only reimburse the product in one indication may have comparatively lower "accessibility" as compared to countries that reimburse it in multiple. *Baricitinib* is used as an illustrative example here (Figure 4.2). However, other products not included in the sample, particularly in the therapeutic area of oncology, would be better examples as they may be approved in upwards of ten

indications. Further to this issue of indications, **adjusting consumption to disease prevalence, which can vary considerably across countries, is particularly challenging and was unable to be achieved in this pilot study.** The possibility of accounting for disease prevalence was explored by reviewing the specific indications in which each sample pair was approved and comparing it to categories used in the Global Burden of Disease Study 2019[25]. However, notwithstanding the issues of considering uptake of alternative products, categories were deemed too broad to be able to estimate prevalence for each product/indication pair.

Figure 4.2. Consumption cannot be disaggregated by indication, which negatively affects interpretation for products with multiple indications

Example: *baricitinib*, used to treat rheumatoid arthritis, atopic dermatitis, and alopecia



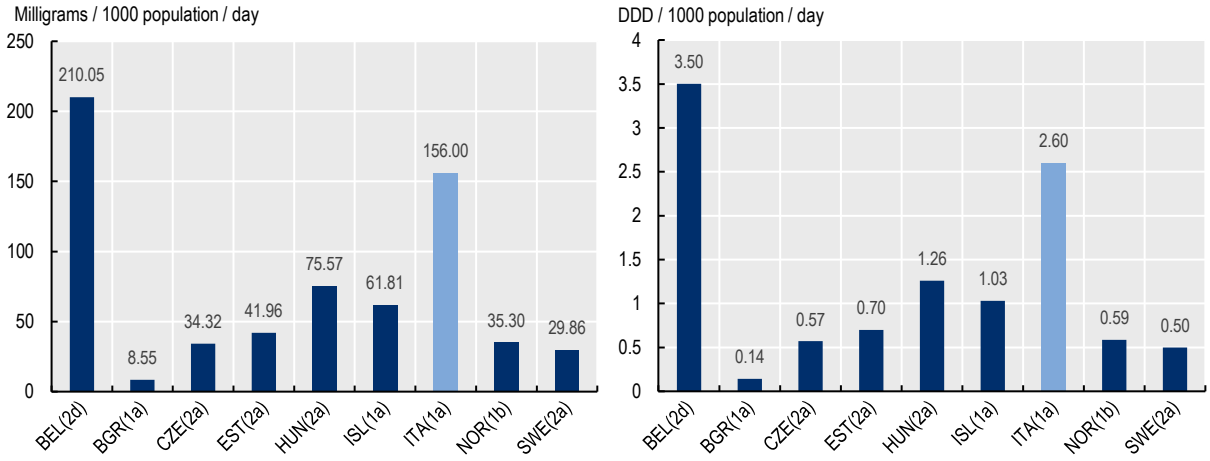
Note: most frequently administered in primary or ambulatory care; most frequently administered in the inpatient setting.
Estimated using total consumption over a yearly period: (a) 12 months prior to 01/10/2021; (b) 2021; (d) 2020.
Source: (1) OECD survey on access to novel medicines; (2) EURIPID database.

87. **Differences in clinical practice, particularly regarding uptake of alternatives, also greatly affect interpretation of comparative utilisation estimates**. Data in the OECD survey were only collected for the sample products, and not any alternatives. However, for those products with one or more alternatives available, comparing consumption only at the product level does not provide any indication about whether a patient has access to *treatment.* For example, *edoxaban* has several alternatives, such as *rivaroxaban* and *apixaban*, that may be used by countries in preference over *edoxaban* (Figure 4.3). This may explain comparatively smaller consumption estimates of edoxaban in some countries than others. **Measuring whether a patient can receive a treatment for which they would benefit would be an arguably better metric of utilisation.** For this, however, it would be important to collect utilisation on the number of patients treated (with any appropriate medicine), in comparison to the disease prevalence, both of which are challenging to collect.

[25] See https://ghdx.healthdata.org/gbd-2019, accessed September 2022.

Figure 4.3. Comparing consumption at product level does not provide any indication about access to treatment if alternatives are available

Example: *edoxaban*, used in the prevention of stroke; treatment of embolism; other alternatives e.g. rivaroxaban, apixaban, dabigatran

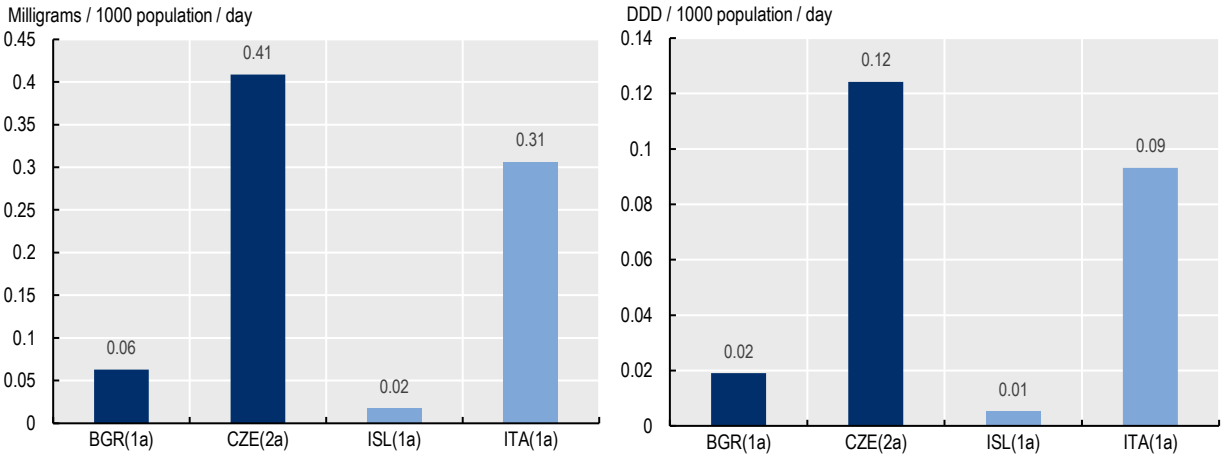


Note: most frequently administered in primary or ambulatory care; most frequently administered in the inpatient setting.
Estimated using total consumption over a yearly period: (a) 12 months prior to 01/10/2021; (b) 2021; (d) 2020.
Source: (1) OECD survey on access to novel medicines; (2) EURIPID database.

88. **The setting of administration determines the likelihood of available consumption data, with inpatient utilisation data less readily available than outpatient data**, particularly if medicines are bundled with costs of care. *Ocrelizumab* is used as an example to demonstrate this issue (Figure 4.4). This is of particular concern for products that may be administered in different care settings in different countries (e.g. inpatient versus outpatient, or both) – see Figure 4.5 for the most frequent setting of administration of each of the products in the OECD survey. Data on inpatient and outpatient use may also be governed by separate entities, such as in Austria and Belgium, further complicating the collection of comprehensive utilisation estimates. Furthermore, system-level factors such as geographical accessibility also play a role in accessibility to patients (Box 4.1).

Figure 4.4. Inpatient consumption data may not be readily available, which may lead to utilisation estimates being underestimated

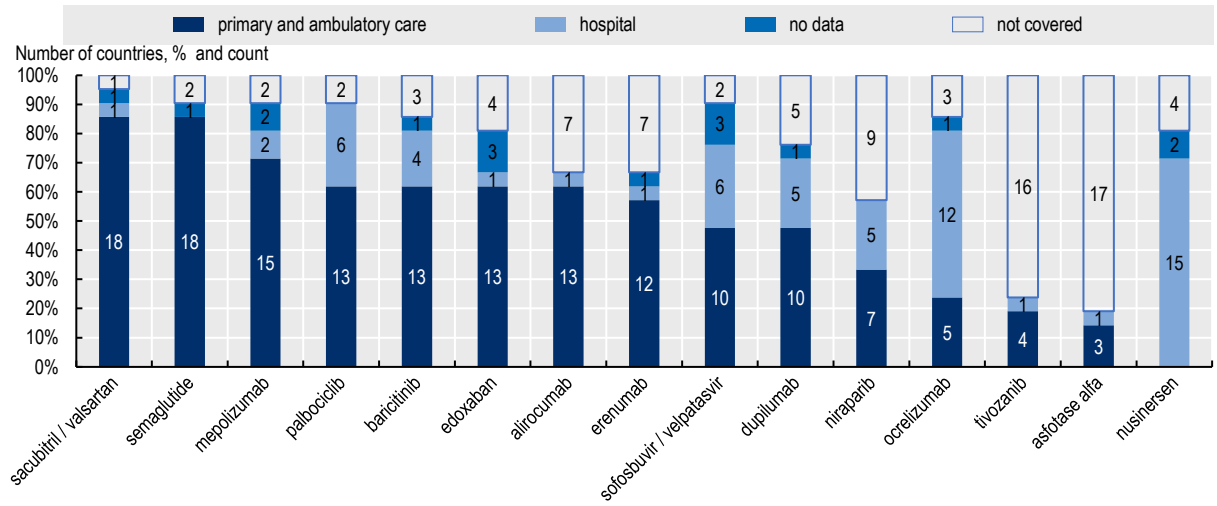
Example: *ocrelizumab*, administered subcutaneously, setting of administration different in different countries



Note: most frequently administered in primary or ambulatory care; most frequently administered in the inpatient setting.
Estimated using total consumption over a yearly period: (a) 12 months prior to 01/10/2021.
Source: (1) OECD survey on access to novel medicines; (2) EURIPID database.

Figure 4.5 Proportion of sample product/indication pairs by setting of administration across countries

Products are administered in different settings in different countries

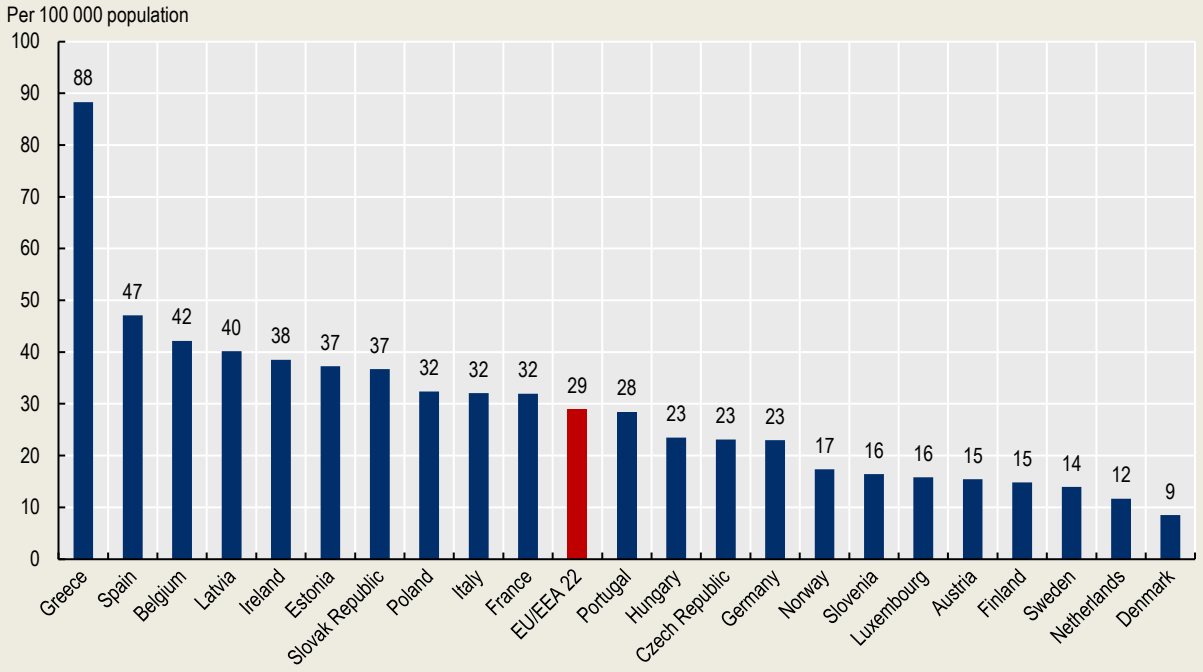


Note: Proportions based on index product/indication pairs that were covered across countries, as at 01 October 2021. Maximum number of countries per product/indication pair was 21. Data labels show counts of countries in each category, per product/indication pair.
Source: OECD survey on access to novel medicines 2021.

Box 4.1. System-level factors such as physical accessibility also play an important role in patient access

System-level factors such as physical accessibility also play a role in accessibility by patients – i.e. geographical closeness to a physician who can prescribe, and to a pharmacist who can dispense, a medicine. In 2019, the overall number of doctors per 1000 population varied across EU Member States, from 2.4 in Poland and 3.0 in Luxembourg, to 5.3 in Austria and Portugal and 6.2 in Greece (OECD, 2021[41]). Numbers for Greece and Portugal may be a significant overestimation as these data refer to all doctors licensed to practice, which includes retired physicians and those who may have emigrated. The number also varies widely across regions, with density generally greater in urban areas. Differences in the density of doctors between urban and rural regions were highest in places like Hungary and Lithuania, and lowest in places like Norway and Sweden. Also in 2019, the number of practising pharmacists varied widely across EU countries – from 21 per 100 000 population in the Netherlands, to more than 120 in Spain, Italy and Belgium. Density of community pharmacies per 100 000 people ranged from 9 in Denmark, to 47 in Spain and 88 in Greece (Figure 4.6). Considerations around geographical accessibility are particularly important for those medicines that may need to be administered in specialised health care settings or hospitals.

Figure 4.6. Density of community pharmacies ranges widely across countries, 2019 (or nearest year)



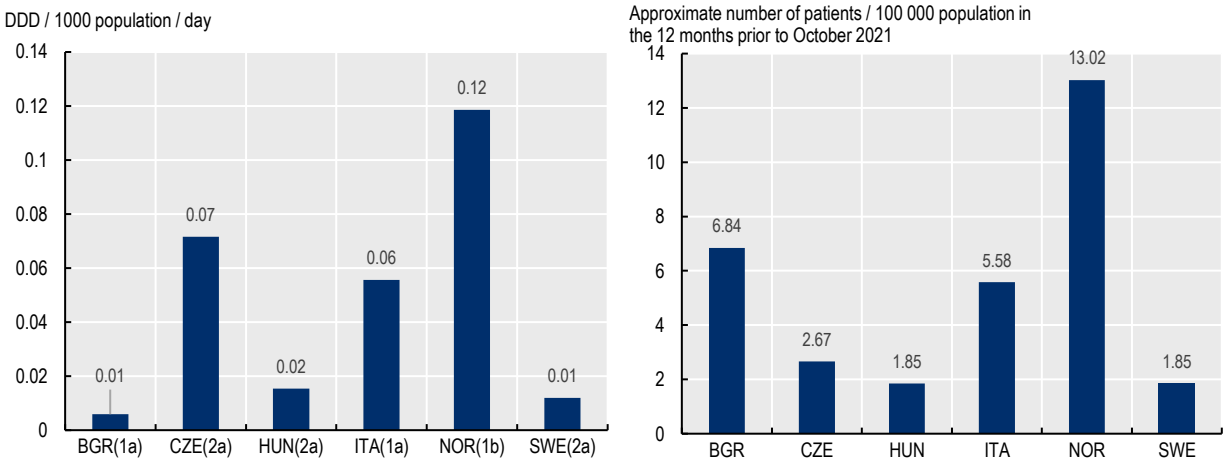
Source: Pharmaceutical Group of the European Union database or national sources for non-European countries, 2019 or nearest year.

4.1.2. Approximate patient numbers can complement other consumption estimates, although further work is needed to enhance comparability

89. Data on approximate number of patients treated can be used to complement other consumption estimates to gain further insight into the access situation in countries, although data may not be internationally comparable at present. The panels in Figure AG.3 in Annex G show the approximate number of patients treated by each medicine in each country per 100 000 population in the 12 months prior to October 2021, where data were available. Despite challenges in comparability of the data specification for "patient number" discussed below, the trend in approximate patient numbers appears to be similar to that seen in the milligrams or DDDs graphs (see Figure 4.7 for an example). For some countries, there was relatively lower consumption and higher number of patients, or vice versa. This likely reflects under-estimation of consumption estimates in some countries, in addition to different data specification definitions.

Figure 4.7. Approximate patient numbers can complement other utilisation metrics

Example: *mepolizumab*, in DDDs / 1000 pop / day, and estimated number of patients per 100 000 pop in the 12 months prior to October 2021



Note: Time periods: (a) 12 months prior to 01/10/2021; (b) 2021.
Source: (1) OECD survey on access to novel medicines; (2) EURIPID database. All patient data comes from (1).

4.1.3. Time series data can be used to show delays in decision-making as well as uptake after granting of coverage

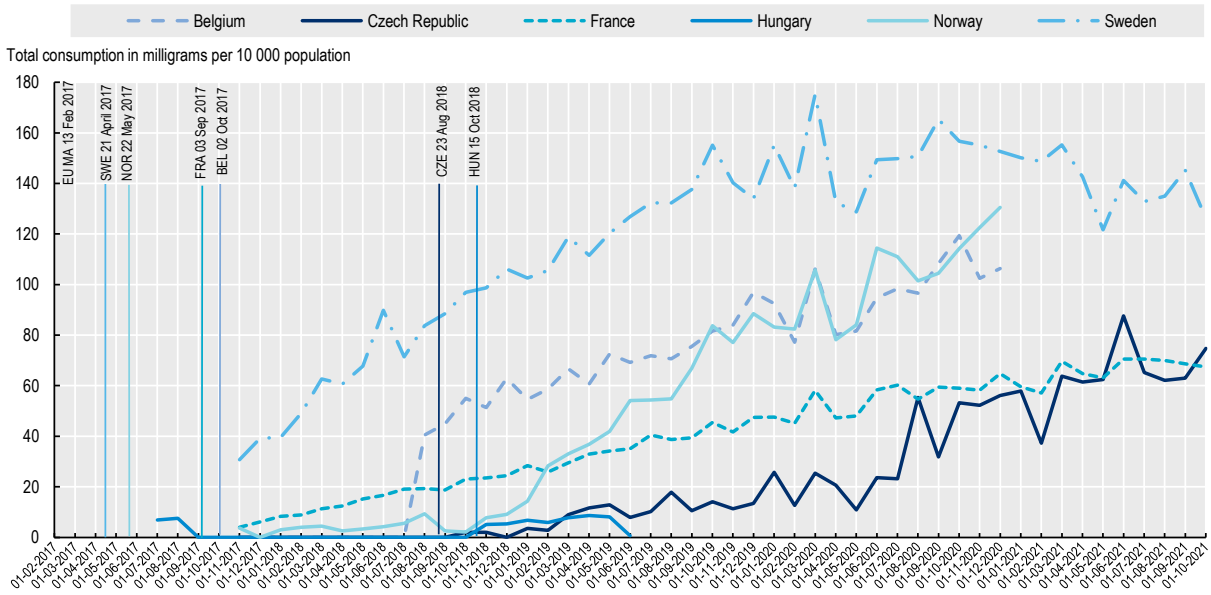
90. The OECD survey only allowed analysis of total consumption data over one point in time to test the feasibility for routine data collection, however time series data provides further insight into patient access. Such data are available for several countries in the EURIPID database, albeit with data gaps depending on data availability. For example, Figure 4.8 shows the total monthly consumption of *baricitinib*, in milligrams per 10 000 population, in several countries from the time of EU marketing authorisation. The date of positive coverage decision is also indicated in the graph. This type of graph can be used to show the **delays in decision-making and subsequent uptake**. It is important to note that sales are possible before granting of coverage in several countries. This can explain consumption data points that appear prior to the positive coverage decision date and can affect interpretation if only analysis on patient accessibility after coverage is desired.

91. **Time series data can also be used to assess uptake.** For example, Figure 4.9 shows the total monthly consumption of *dupilumab*, in milligrams per 10 000 population, for the 24-month period after

granting of coverage in several countries. This type of metric can give insight into patient accessibility after the granting of coverage, notwithstanding the many caveats previously discussed, such as availability of alternatives.

Figure 4.8. Time series consumption data can be used to show delays in decision-making and patient access

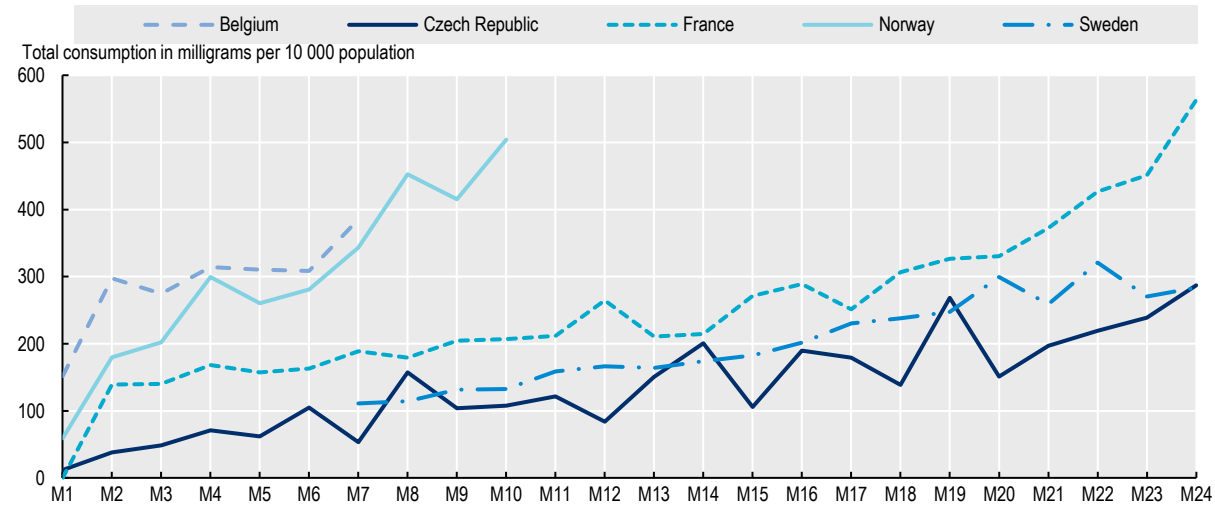
Example: Total monthly consumption of *baricitinib* in milligrams per 10 000 population, from EU MA date



Note: Time series from date of EU marketing authorisation, indicating positive coverage decision dates in each country. In the case of Hungary, volume data for baricitinib has not been shared with EURIPID since July 2019.
Source: EURIPID database, 2021.

Figure 4.9. Time series consumption data can be used to show uptake after granting of coverage

Example: Total monthly consumption of *dupilumab* in milligrams per 10 000 population, 24 months after positive coverage decision



Note: M1 = the first month after positive coverage decision. Data gap from month one to seven in Sweden, and after month seven and ten in Belgium and Norway, respectively.
Source: EURIPID database, 2021.

4.2. Both comprehensive and comparable data on consumption and approximate patient numbers are challenging to identify

92. **Comprehensive volume data are not generally publicly available, and in some cases are considered commercially sensitive**, **hindering the feasibility of generating routine metrics**. A recent publication by Vogler (Vogler, 2022[39]) found that public access to volume and sales data is mixed across the WHO European region; for example, these data are publicly accessible in several countries, although sometimes only for those medicines that are publicly funded. The scope of data to which the public and national authorities have access to is also limited, while companies have volume and sales data on all the products they sell. Some countries share data via websites or in annual reports, but usually at an aggregated level (e.g. by disease area). While information at the level of the individual active substance, as collected in the OECD survey, can support policy makers regarding monitoring and decision-making, data are not always able to be published at this disaggregated level. Despite this, over half of responding countries to the OECD survey were able to submit estimates for the index products that were covered and had been sold in their respective countries as at 01 October 2021 (see Table AG.1, Annex G). International comparability, however, is challenged by the different data sources used by countries, including sales data, wholesale reports, prescription data, dispensing data, reimbursement claims data etc[26]. Utilisation data may be even more challenging to obtain for some orphan or ultra-orphan products in some countries, if they are, for example, provided through an alternative access mechanism. In addition, as compared to other access metrics which may be updated continuously or monthly, utilisation data may only be available with a time-lag or on a quarterly (e.g. Czech Republic, Estonia) or yearly basis (e.g. Norway).

93. **Similarly, data on approximate number of patients treated are not readily available in some countries.** Less than half of responding countries were able to provide an approximate indication of this metric (Bulgaria, Czech Republic, Estonia, Greece, Hungary, Italy, Norway, Sweden - see Table AG.1, Annex G). In others, these data were not provided. For example, Belgium was unable to answer this question as it does not have a complete overview regarding this subject. It only has data for public pharmacies and not use in hospitals, however these data are governed by an external body for which access permission is required, and data have a general reporting delay of around six months. In Iceland, information on the number of patients is not accessible. In Greece, while these data are available, they are considered commercially sensitive.

94. To **enhance the international comparability of both types of indicators, further work on standardising survey data collection and data specification would be required.** Utilisation estimates need to be collected as **total utilisation, regardless of pharmaceutical strength, form, or pack size**, in **milligrams** or **defined daily dose,** as data in total number of units (or packages) sold does not allow for cross-country comparisons.

- For DDDs, an indication of the DDD used (WHODDD or own definition e.g. prescribed daily dose) also needs to be included. If an active substance has more than one DDD (e.g. oral versus intravenous form), estimates of total consumption for both would need to be provided. Some issues with using DDDs as a unit of measurement were previously described[24].
- In the case of approximate patient number, differing definitions of the term 'patient' hamper international comparability. For example, the Estonian estimates refer to the number of inhabitants

[26] The 2019 OECD analytical report and EU/EEA country notes on *Using Routinely Collected Data to Inform Pharmaceutical Policies* found that the main sources of routine data on prescribed or dispensed medicines in OECD and EU member states include pharmacy records (i.e. information on mostly outpatient medicines that have been dispensed to patients), reimbursement claims and billing information, and personal health records. Many countries monitor trends in consumption and spending at national level. See the report and country notes, both available at https://www.oecd.org/health/health-systems/routinely-collected-data-to-inform-pharmaceutical-policies.htm, last accessed July 2022.

who may have used the medicine in DDD every day during the 12-month period indicated in the questionnaire, while the Swedish estimate refers to the number of people who have picked up a medicine at least once a year or month (with estimates on a yearly basis).

95. Overall, the **OECD survey highlighted some of the major issues with collecting, interpreting, and presenting data on consumption of individual medicines, as has already been noted in other studies**. Volume data are not often available in the public domain (or are even considered commercially sensitive), or at a level of disaggregation that would better aid analyses. Use of existing platforms, such as EURIPID, could be leveraged to better capture volume information. EURIPID collates consumption data from several countries on a monthly basis for mostly outpatient products, although there is a reporting delay in receiving timely volume data from countries. A benefit of using existing databases, such as EURIPID, over survey data is that significant work has already been done to standardise the dataset, as well as to develop an understanding of the sources used by countries to provide these data. Should further work around consumption estimates be of interest to countries, importance should be placed on exploring the possibility of generating a more meaningful metric (i.e. whether or not a patient receives the treatment for which they would benefit) with detailed data specifications to better enhance international comparability. Interestingly, a recent IQVIA (2022[42]) publication explored the relative use of 20 selected groups of 107 novel medicines across Europe. Medicines were analysed in groups in an attempt to account for the existence of alternatives, rather than assessing the accessibility of individual medicines. Further study details are outlined in Table AB.1, Annex B).

5. Acceptability dimension: measures are less well defined and not assessed routinely

96. Product/indication-level indicators of acceptability are less well defined in the literature but can be used to better understand patterns of clinical use (see Section 1.1.4). The extent of inclusion of a product in a given indication in clinical guidelines and/or treatment protocols can provide some insight into the acceptability of a product within a country market (Section 5.1). Perceived "added" therapeutic value is another measure that may influence the acceptability of a medicine (Section 5.2). Acceptability also depends on the presence of available appropriate alternatives, which has already been explored in Section 2.

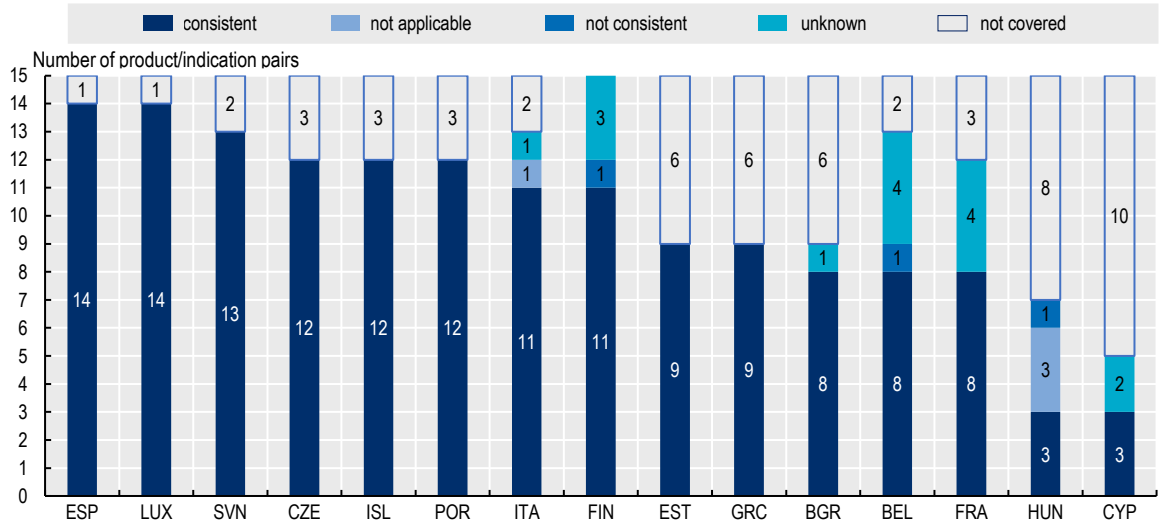
5.1. Extent of inclusion in therapeutic guidelines can be a proxy of acceptability, but data are neither assessed routinely nor readily available

97. Extent of inclusion in clinical guidelines or treatment protocols in comparison to the coverage decision can give an indication of the acceptability of the product. In almost all cases with available data, responding countries indicated that the use of the covered product/indication pairs as recommended in national clinical guidelines or treatment protocols was consistent with the covered indication (Figure 5.1). Therefore, it was not possible to further examine the possible reasons behind issues of concordance. Consistency with clinical guidelines did not appear to be medicine-dependent, with use of most products considered consistent with the covered indication in most countries.

98. **However, these data on guideline versus coverage consistency are not routinely assessed by countries**. Responding countries used a variety of sources to collect information on this topic, such as various websites and published clinical guidelines (e.g. Czech Republic, France), therapeutic protocols available on the Ministry of Health websites (Greece), clinical hospital guidelines (Hungary, Iceland), and protocols produced by the National Pharmacotherapy Committee (Portugal). Also, guidelines are generally disease specific and may be developed at international, national, regional, or even institutional level. One respondent mentioned that it would require a lot of time and effort to assess this metric. In addition, some countries reported that clinical guidelines were not updated regularly, so it may take some time between a product being granted coverage and its appearance in a national guideline. Despite these challenges, at least 15 of the 21 responding countries were able to provide data for most of their covered products. Some countries were not able to provide these data for any (Lithuania, Norway, Sweden), or all of their respective covered products (Belgium, Bulgaria, Cyprus, Germany, Finland, France). Further consideration needs to be given to the utility of this metric, given the challenges encountered in gathering internationally comparable data.

Figure 5.1. Proportion of sample product/indication pairs by consistency between coverage and clinical guidelines across countries

National treatment guidelines were generally consistent with covered indications



Note: : Proportions based on sample of 15 index product/indication pairs, in 21 responding countries, as at 01 October 2021.
Answer to the question "Is the use of this product as recommended in national clinical guidelines or treatment protocols consistent with the covered indication?". As at 01 October 2021. Lithuania, Malta, Norway and Sweden were not included due to data availability. Austria and Germany indicated that this is not applicable in their countries.
Source: OECD survey on access to novel medicines 2021.

5.2. Simple measures can be used to compare HTAs and assessments of "added" therapeutic value, but may be insufficiently granular

99. **While broad access to all medicines is often assumed to be ideal, it may not in fact be essential**. The importance of a medicine for a country depends on a number of factors including the burden and severity of disease, benefits offered by the medicine relative to the existing standard of care, and the availability of appropriate alternatives in sufficient quantities. An appropriate alternative may be within the same therapeutic class or a different class, but within the same indication. Linked with this is the idea of therapeutic "added" value, which refers to the incremental effectiveness of a product over standard care. HTA agencies often reach different conclusions on added therapeutic value and cost-effectiveness of products, which may arise from differences in data interpretation, or may reflect differences in for example, the population burden of disease, demographics, prevailing standards of care, resource utilisation, and willingness to pay.

100. While the OECD survey was not able to elicit the perceived therapeutic value of each medicine in the sample in each responding country, respondents were asked whether the most recent HTA outcome was positive or negative, whether the product/indication pair was considered to offer added therapeutic value over alternatives, and what degree of added therapeutic value was identified. Exploration of therapeutic value could only be undertaken in a subset of cases (75 of the total 315 country-product/indication pairs), for which there was an HTA outcome, and where the most recent HTA submission reflected the first (or initial) submission for assessment. This was to ensure better comparability of data across countries, as subsequent HTA reports may reflect submissions for subsequent indications (e.g. *baricitinib* in the OECD survey was originally indicated in rheumatoid arthritis, while subsequent HTA submissions were for use in atopic dermatitis).

101. Table 5.1 shows the differences across countries in the initial HTA outcome for the sample product/indication pairs, as well as the considered added therapeutic value offered over alternatives. The number of countries for which HTA outcomes could be analysed per product/indication pair was small, and ranged from two for *alirocumab*, to eight for *mepolizumab.* Nevertheless, in most cases in the analysed subset, the assessment was positive (67 of 75 cases), with more than a third of these (45 of 67) citing added therapeutic value over alternatives. **Each of the 15 product/indication pairs had received a positive HTA in at least two countries**. For some products, countries gave different assessments – either negative or positive (e.g. for *asfotase alfa, erenumab, mepolizumab, nusinersen*, and *tivozanib*). Positive or negative recommendations are not always given in some countries (e.g. in Sweden for inpatient medicines) or not sufficient to describe the outcome of the HTA evaluation.

102. **Comparisons between the determined *level* of therapeutic value for a product/indication were difficult to make across countries using survey data**, due to differences in country classifications. In Belgium and Greece, for example, no specific level or class of therapeutic value is used. In Hungary, describing the extent of added therapeutic value is implemented in HTA reports as of 2022. Bulgaria, Norway and Sweden express added value in quality adjusted life years (QALYs) and life years gained (LYG). Estonia, France, Italy, Portugal, Slovenia, and Spain reported the extent of added therapeutic value using some sort of scale (e.g. minor, moderate, major, significant, very significant, important, intermediate etc), but these metrics are not standardised across countries. Other countries expressed added value in terms of specific subpopulations or by effect on specified clinical endpoints (e.g. progression free survival, reduction in symptoms etc).

103. **Positive HTA outcomes did not necessarily result in publicly funded coverage.** In more than 85% of cases, a positive HTA led to a positive coverage decision. In most cases with both a positive HTA and a determination of added therapeutic value, the product was covered for the indication in question (38 of 4). In the remaining seven cases, either a coverage determination was still in process or had been denied, or exceptional reimbursement on a case-by-case basis was available. Three of the eight cases with a negative HTA result were still covered, two of which were considered to have added value over alternatives, and one without.

Table 5.1. Initial HTA outcome and considered added therapeutic value of the sample products over alternatives

More than a third of positive HTAs cited added therapeutic value over alternatives

Outcome in the HTA report:	Negative HTA (n=8)		Positive HTA (n=67)		*Total (n=75)*
Added therapeutic value over alternatives:	No added therapeutic value	Added therapeutic value	No added therapeutic value	Added therapeutic value	
alirocumab			1	1	***2***
asfotase alfa[1]		1	1	1	***3***
baricitinib[2]			3	1	***4***
dupilumab				7	***7***
edoxaban			4		***4***
erenumab[1]	1		2	4	***7***
mepolizumab	1		3	4	***8***
niraparib			1	2	***3***
nusinersen[3]	1	2		3	***6***
ocrelizumab[1]				5	***5***
palbociclib			1	3	***4***
sacubitril / valsartan				4	***4***
semaglutide			3	5	***8***

Outcome in the HTA report:	Negative HTA (n=8)		Positive HTA (n=67)		*Total (n=75)*
Added therapeutic value over alternatives:	**No added therapeutic value**	**Added therapeutic value**	**No added therapeutic value**	**Added therapeutic value**	
sofosbuvir / velpatasvir			2	3	***5***
tivozanib[2]	2		1	2	***5***
Total (n=75)	***5 (7%)***	***3 (4%)***	***22 (29%)***	***45 (60%)***	***75 (100%)***

Note: Count refers to number of countries. The table should be read as follows: e.g. *mepolizumab* – one country reported a negative HTA and stated that it did not offer added therapeutic value over alternatives; 3 countries reported positive HTAs despite no finding of added therapeutic value over alternatives; 4 countries reported positive HTAs and added therapeutic value over alternatives.
1. One country did not provide a response for the question on HTA, but reported that the product was considered to have added therapeutic value over alternatives. 2. One country did not provide a response for the question on HTA, but reported that the product was not considered to have added therapeutic value over alternatives. 3. One country did not provide a direct response regarding HTA or therapeutic value due to large uncertainties about long term effects.
Source: OECD survey on access to novel medicines 2021

104. **Cross-country comparisons of HTAs and assessments of added therapeutic value are difficult**, as **data are generally not publicly available** and simple metrics such as those used in this survey (e.g. positive / negative / yes / no) are generally inadequate to describe country assessments. Section 2.1.4 describes some of the challenges in collecting standardised data related to HTA processes. Nevertheless, most countries that utilise HTA were able to provide an indication of the eventual outcome. Most were also able to provide an indication of added therapeutic benefit.

6. Lessons learned and next steps

105. The overarching aim of this project was to determine the utility and feasibility of systematic and periodic cross-national monitoring of access to new medicines across the dimensions of availability, affordability, accessibility, and acceptability. The findings highlight the value of using a broader set of indicators and looking at access across multiple dimensions. However, while it was possible to generate an expanded set of indicators and to take into account other contextual factors, the results can nevertheless be misleading, and the feasibility of routine monitoring is hampered by the current data landscape. In general, most countries that responded to the OECD survey do not systematically measure or monitor access to medicines on a product/indication basis (see Table AD.4, Annex D). Those few that do, monitor progress of processes (such as HTA, coverage, and pricing and formulary listing decisions), or measures of consumption and expenditure. For example, both Belgium and Portugal have internal databases to support such processes, but this information is not publicly accessible. Drawing on data collected via the OECD survey as well as lessons learned throughout this process, the sections below discuss further methodological considerations (Section 6.1), and next steps (Section 6.2).

6.1. Developing aggregate access indicators is challenging and not possible for every dimension

106. Several aggregate availability indicators were produced (of which four related to measuring different time periods) and two aggregate acceptability indicators. However, while two product-level indicators were produced for the dimensions of affordability and accessibility, aggregate indicators were not possible as price and consumption data could not be aggregated across the heterogenous study sample. Consequently, no attempt was made to create a single composite indicator.

107. Figure 6.1, however, provides an example of an analysis across the four dimensions for one medicine, *dupilumab.* As of 01 October 2021, *dupilumab* was covered and sold in the atopic dermatitis indication in most responding countries (15 of 21). However, only in Germany was the covered indication as broad as the approved indication, without additional limits or restrictions on coverage. In all other countries, the covered indication was narrower than the approved indication, and most of those countries also placed additional restrictions or limitations on coverage. Affordability to the health system varied across countries. While the product was available free of charge in several countries, among those where patient contributions applied, the highest financial burdens were seen in Finland, followed by France, both of which structure cost-sharing in the form of coinsurance. Consumption data show that utilisation varied widely across countries, which may reflect differences in clinical practice or burden of disease. Lastly, the use of *dupilumab* according to national clinical guidelines was generally consistent with the covered indication.

Figure 6.1. Example: access to *dupilumab* across the four dimensions using selected indicators

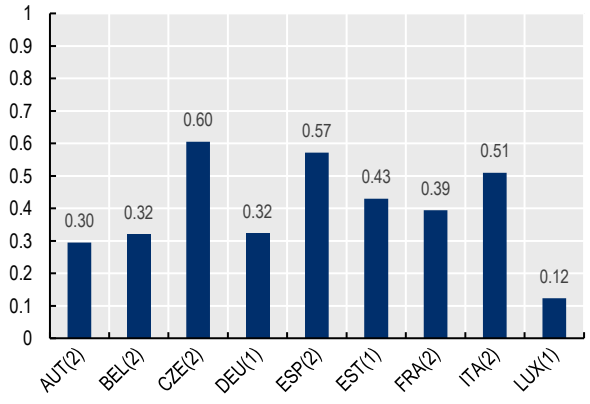
Availability, 01 October 2021

Country	AUT	BEL	BGR	CYP	CZE	DEU	ESP	EST	FIN	FRA	GRC	HUN	ISL	ITA	LTU	LUX	MLT	NOR	POR	SVN	SWE
Overall availability			–	–							–	–					–				
Extent of coverage in comparison to MA																					
Additional coverage restrictions																					

Overall availability: covered and sold; covered and sales unknown; covered and not yet sold; HTA evaluation and/or coverage decision in process; no HTA dossier and/or coverage application submitted; coverage denied or HTA evaluation and/or coverage decision did not proceed. (-) no alternatives available.
Extent of coverage in comparison to MA: full scope = covered indication not narrower than the EU authorised indication by (1) patient population or subgroup, (2) duration or quantity of treatment for individual patients, or (3) prerequisite of failure of (or intolerance to) a prior therapy; limited scope = covered indication narrower than the EU authorised indication by at least one of categories (1), (2) or (3).; extent of scope unknown; not covered
Additional limitations and restrictions on coverage: no limits or restrictions = coverage not restricted by (1) requirement for demonstrated response to treatment; (2) maximum number of patients per annum; (3) prescriber type; or (4) other. some limits or restrictions = coverage restricted by at least one of categories (1), (2), (3) of (4). limits or restrictions unknown; not covered.

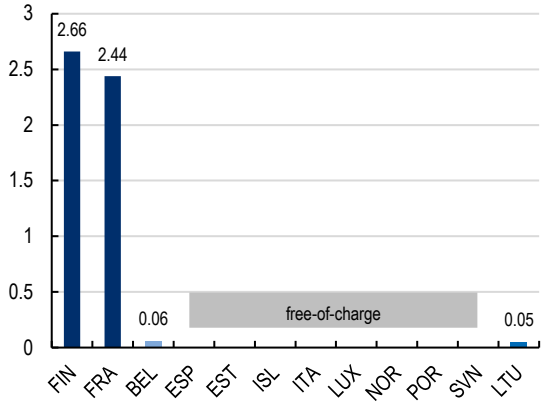
Affordability

System: *Cost per year of treatment relative to GDP per capita, using ex-factory prices*



Source. (1) OECD survey (2) EURIPID data

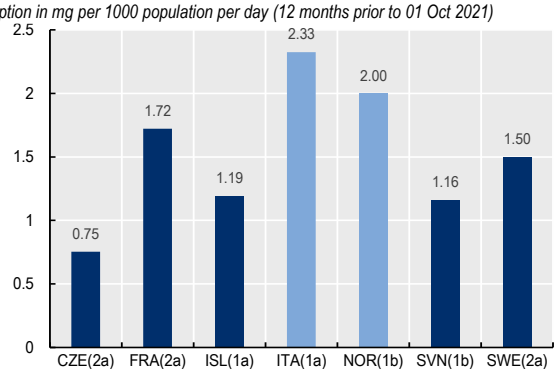
Patient: *Out-of-pocket costs for one month of treatment relative to average daily wage*



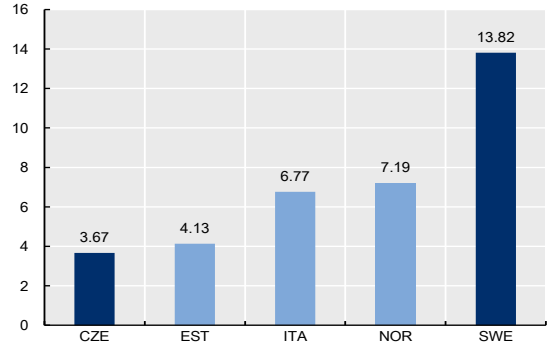
coinsurance, fixed co-payment, other (e.g. deductible, extra-billing).

Accessibility

Consumption in mg per 1000 population per day (12 months prior to 01 Oct 2021)



Approximate number of patients per 100 000 population (12 months prior to 01 Oct 2021)



most frequently administered in primary or ambulatory care, most frequently administered in hospitals; (1) OECD survey (2) EURIPID data. (a) 12 months prior to 01/10/21 (b) 2021.

Acceptability, 01 October 2021

Country	AUT	BEL	BGR	CYP	CZE	DEU	ESP	EST	FIN	FRA	GRC	HUN	ISL	ITA	LTU	LUX	MLT	NOR	POR	SVN	SWE
Consistency with national guidelines																					

consistent; not applicable; not consistent; unknown; not covered

Source: OECD survey on access to novel medicines 2021.

6.1.1. Data come from multiple sources of varying quality and confidentiality

108. A wide variety of data sources were used by responding countries to provide the information requested in the OECD survey, which covered seven different domains (A. early access schemes; B. HTA; C. coverage and pricing; D. treatment costs; E. prescription; and F. utilisation) (see Table AD.4 and AD.5, Annex D). Most countries do not have a centralised database but hold these data across various institutions, including ministries of health, national medicine regulatory agencies, pricing and reimbursement entities, insurance agencies / funds, pharmacist, and hospital associations etc.

109. In most cases, the requested survey data were only partially publicly available, and some respondents drew on additional (at times, confidential) internal data sources. Moreover, publicly available data were not always readily accessible or downloadable in a standardised format, and included information from public websites, in searchable online databases, or in downloadable PDF or Microsoft Excel files.

110. Despite the multitude of data sources used and differences in health care systems, almost all responding countries were able to provide nationally representative data as at a specific date, 01 October 2021, including those countries with decentralised systems, such as in Sweden and Norway. In Austria, data for all outpatient product/indication pairs were nationally representative while four regions reported available data for hospital products. Utilisation data were the most challenging to obtain, either due to data unavailability or delays in publication or reporting. While some countries were able to provide these data, for legal reasons they may not be disclosed publicly at the level of the individual active substance.

111. The feasibility of routinely collecting this quantum of complex and detailed information at the product/indication-level, however, would be hampered by the large variety of data sources and relevant institutions involved. Future analyses could focus on publicly available data as a priority, and on information already gathered in other databases (such as EURIPID).

6.1.2. There are several methodological issues to consider for future analyses

112. Various challenges in the collection and interpretation of these data and potential confounders have already been described in this paper, but some of the main issues are also summarised in Table 6.1 and below.

113. In some cases, data at the level of the indication were not available at all (e.g. utilisation data), or only available in some countries. In order to limit the impact of this, efforts were made when first selecting the sample of 15 product/indication pairs in this pilot to preference those with a single principal indication. Despite this, there were cases where a product was covered in a subsequent indication and thus data may not be comparable across countries. Conversely, collecting, and interpreting information at product (rather than indication) level can also compromise comparability, if products are covered in one indication in some countries, and in additional or different indications in others.

114. The selection of the 15 sample product/indication pairs also favoured products predominantly administered in an ambulatory care setting because of the greater likelihood of data availability. However, many novel products are used in an inpatient setting, or the setting may vary at regional or institutional level. Furthermore, the sample selection favoured products without mandatory co-administration, so that access would not depend on the availability of one or more other products. In reality, many products, especially in disease areas such as oncology, require co-administration and this would require further consideration.

115. Significant data gaps and a small heterogenous sample were among the other key challenges in exploring different indicators and developing cross-country comparisons. As noted previously, indicators of access are influenced by both country-specific and medicine-specific issues. The small sample size and heterogeneity hampered the ability to explore these further. In further work, the grouping of products into

different archetypes (e.g. orphan status, disease group, setting of administration etc) or therapeutic areas could be considered.

116. **Indicators of access and their interpretation are compromised by the availability of data and the uncertain impact of different health care system characteristics**. This is especially relevant when analysing data for medicines that are administered in different settings, as the systems (and data availability) in each country may differ between inpatient and outpatient medicines. Cross-country comparisons may potentially be facilitated by grouping countries with common health system characteristics that could affect specific indicators. This would also facilitate a greater understanding of the relationship between health system characteristics and measures of access. Further exploration of this issue is needed.

Table 6.1. Challenges in collection and interpretation of product/indication-level data across dimensions

Challenge	Affected dimensions and metrics
Products may have appropriate alternatives, either within class or within indication.	**Availability:** Collecting data on availability of a particular medicine does not take into account the existence of appropriate alternatives, either within class or within indication. This means that a patient may not be disadvantaged if a particular medicine is not available. In some countries, products are procured competitively within class or by indication. **Acceptability:** Depending on which products are covered / reimbursed for an indication in a given country, the priority order of treatment may vary. **Accessibility:** Utilisation / consumption data were only collected for the sample products, and not for alternatives. Measuring whether a patient is able to receive a treatment for which they have a need would arguably be a better metric of utilisation.
Products can be of a different archetype (e.g. orphan medicines, approval under exceptional circumstances, accelerated approvals, advanced therapy medicinal product), and these archetypes may go through different in-country processes.	**Availability:** Orphan products used in rare diseases, or those products used to treat diseases with high unmet need for which there are no or a limited number of alternatives, may be treated differently to other products. For example, in some countries there are different HTA or coverage/reimbursement procedures for orphan products[1]. In other countries, early access schemes may provide accelerated access - either prior to marketing authorisation or granting of coverage - for a limited number of patients or to the entire target population within the scope of an indication. Other countries, particularly those with small markets, may only provide access to these products via alternative access mechanisms such as on an individual named-patient basis. This may be because there may be too few expected patients for the marketing authorisation holder to have an interest in submitting an application, or for the country to undergo the general coverage evaluation process. These alternative mechanisms are not captured via current availability metrics. **Affordability:** Affordability estimates at both the system and patient level are affected by the funding of alternative access mechanisms. In some cases, funds may be earmarked for a specific disease or therapeutic area. **Acceptability:** Medicines that are not granted coverage in the traditional sense, e.g. via inclusion in a positive list, may not be included in clinical guidelines. **Accessibility:** Utilisation data may be unavailable if a product is provided via a patient access scheme.
Some products have more than one primary indication, and countries may not cover the product in all its approved indications.	**Availability:** Care needs to be taken to ensure that availability metrics reflect availability in the specified indication. **Affordability:** Price comparisons may be affected where indication-based pricing applies. **Accessibility:** It may not be possible to disaggregate utilisation / consumption by indication. It is also challenging for most countries to provide utilisation estimates for the inpatient sector.
Products may be administered in different care settings in different countries (e.g. inpatient versus outpatient, or both).	**Availability:** Availability of a particular medicine may vary within countries and across care settings. **Affordability:** Estimates of affordability to the patient for inpatient medicines may be challenging to discern, depending on funding and cost-sharing mechanisms, particularly if medications are bundled with costs of care in inpatient settings. Affordability estimates will also be affected if cost-sharing is different according to the care setting. **Acceptability:** Use of a medicine in an inpatient setting may depend on institution specific guidelines. **Accessibility:** It is challenging for most countries to provide estimates for the inpatient sector. Data on inpatient and outpatient use may be governed by separate entities.
Some products require mandatory co-administration of another product.	**Availability, acceptability, accessibility:** These may depend on the availability, acceptability, and accessibility of the co-administered product(s).
Some products go through more than one round of submission or application for HTA or reimbursement for a particular indication, for example if coverage has initially been denied.	**Availability:** From the data collected in the survey it is not necessarily possible to discern whether or not a product has been subject to multiple submissions. Decomposed time-to-access metrics may be affected by the presence of multiple submissions, particularly where a product is initially rejected and then granted coverage after a subsequent application.

Challenge	Affected dimensions and metrics
Products may be sold before they receive marketing authorisation or are granted coverage in each country.	**Availability:** Alternative access mechanisms in some countries may allow for a product to be sold prior to marketing authorisation or coverage. However, it may not be possible to distinguish reimbursed versus non-reimbursed sales in utilisation data. As such, availability metrics based on whether or not a product is sold do not necessarily reflect access for the general population. Similarly, date of first sale may be a poor proxy for access to the general population, unless it is after the date of positive coverage decision. **Accessibility:** See "Availability".
Pharmaceutical products with the same active substance come in multiple presentations (i.e. based on strength, pharmaceutical form, and pack size). Countries may have different presentations available.	**Affordability:** Price comparisons generally need to be made on a "like for like" basis for individual medicines i.e. at the level of the strength, pharmaceutical form, and pack size. **Accessibility:** Utilisation estimates need to be collected regardless of pharmaceutical strength, form or pack size, in milligrams or defined daily doses. If data are provided in number of units sold, then the underlying disaggregated data by strength/form/pack size also need to be available to be able to estimate monthly or annual consumption.

Note: 1. See IMPACT HTA's country vignettes on HTA appraisal/reimbursement processes for rare disease treatments https://www.impact-hta.eu/country-vignettes , accessed July 2022.
Source: Authors, based on experience gathered through the OECD survey on access to novel medicines 2021.

6.2. Further work requires prioritisation of indicators and methodological standards for collection and comparison

6.2.1. Routine collection using this approach would be highly complex

117. This exercise has highlighted challenges in identifying, collecting, and interpreting data on access to medicines at the product/indication-level across multiple dimensions. In general, while it is possible to collate such detailed data, it is both challenging and time consuming to collect and interpret even on a small scale, and thus repeated, routine collection across dimensions via existing survey methods may be impractical. Significant additional and complex methodological work would be required to develop a single metric for each domain, or an index of overall access suitable for regular measurement and reporting.

118. As mentioned in previous sections, the outputs of this analysis are of limited interpretation value given the small heterogenous sample, however, the routine collection of data across access dimensions for a larger sample would not necessarily enhance representativeness. The small sample size in this exercise allowed for manual adjustment of data to better reflect the access landscape in cases where existing confounders could not easily be quantified. For example, while criteria-based safety nets or caps on out-of-pocket costs were difficult to quantify and therefore generally excluded from the analysis (see section 3.2.2), Finland's annual cap was taken into account. With a larger sample, it would become more challenging to make such individual adjustments. Moreover, this analysis demonstrated that some confounders are dependent on the medicine archetype. Hence, conducting a similar analysis on a larger scale would likely magnify existing confounders as the number of different medicine archetypes in the sample would increase.

119. Section 4.1.3 also highlighted the limitations of cross-sectional data and signalled that time-series data could be of more value to policymakers, especially for the dimension of accessibility. Given the feasibility challenges in collecting data on a small scale, data from existing databases, such as EURIPID, could be used wherever possible to explore time-series data. For example, Figure 4.8 and Figure 4.9 demonstrate how time series consumption data from EURIPID can be used to show delays in decision-making and patient access, and uptake after granting of coverage, respectively.

6.2.2 Next steps should focus on developing consensus around those indicators deemed most relevant and comparable, and standardising the methodology for their collection and interpretation

120. Further development or expansion of this work beyond this pilot study would benefit from the following, while also recognising that there will be an inherent trade-off between accuracy, comprehensiveness and feasibility of any indicators produced moving forward:

- **Greater clarity around the objectives of monitoring and measurement of access**, and consideration of whether other approaches may be more appropriate. Most countries that responded to the survey do not systematically measure or monitor access to medicines on a national level; of those that do, some focus on the efficiency of processes, others on measures of overall consumption or expenditure. A **multistakeholder consultation** could be used to take stock of the lessons learned in this and other studies to develop consensus around what should be measured routinely to inform policymakers. Where possible, consideration could be given to, whether measuring "access to treatment" as distinct from access to individual medicines may be more appropriate, noting that while broad access to all medicines is often assumed to be ideal it may not in fact be essential.
- **Agreement on the indicators that should then be prioritised**. Some indicators are more suitable for routine collection than others, such as those with data in the public domain or in existing sharing platforms. Going forward, it will be important to develop some consensus on the indicators of highest priority, utilising criteria such as such as relevance, actionability, feasibility, comparability etc, as has been done in previous research (World Health Organization, 2019[43]; Carinci et al., 2015[44])
- **Agreement on the scope of analysis for periodic assessment.** Analyses may need to distinguish between outpatient and inpatient products, or consider them separately, given the differences in country processes and data availability. Some indicators may be more appropriate for measuring access to a medicine archetype or therapeutic class, rather than an individual medicine. For example, an analysis of access to breakthrough therapies used in the treatment of rare diseases could be appropriate, given that these products may be subject to exceptional evaluation processes.
- **Development of agreed methods for collecting, exchanging, and interpreting data,** with consideration of individual country contexts. Taking into account the structure of the health care system, and the regulation, selection, coverage and pricing policies in place, can help in framing and interpreting the results. While it may not be possible to control for these factors, cross-country comparisons could be facilitated by grouping countries with common health system characteristics that could affect specific indicators. Extensive contextual information already available in other platforms could be leveraged and triangulated with any quantitative measures.
- **Investment in improving the evidence base,** which involves the willingness of countries to systematically collect and share the necessary data in a timely manner. The lack of transparency in the area of pharmaceutical coverage, pricing, and utilisation not only hinders the routine analysis of data, but also the generation of reliable evidence to inform important policy questions. Where possible, priority indicators should draw on existing data sources (including existing international data sharing platforms), and where these are unavailable, they should be a priority for development.

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