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Challenges in access
to oncology medicines:
Policies and practices
across the OECD and the
EU

**Suzannah Chapman,
Valérie Paris,
Ruth Lopert**

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**CHALLENGES IN ACCESS TO ONCOLOGY MEDICINES
Policies and practices across the OECD and the EU**

Suzannah Chapman*, Valérie Paris*, and Ruth Lopert*

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Abstract

Expenditure on oncology medicines is steadily increasing, not only due to the magnitude of launch prices, but also to growth in the number of patients being treated (a combination of increasing prevalence, new treatment options, prolonging survival and extending the duration of treatment). Rapid therapeutic advances in oncology and the desire to facilitate speedy access to promising new treatments are together creating challenges to even the wealthiest countries' capacity to provide – and sustain – affordable access. These challenges include the often-significant uncertainty surrounding the degree of clinical benefit offered by new medicines at the time of market entry and coverage determination, as well as the complexities of determining price and place in therapy of products with multiple approved indications reflecting variable degrees of clinical benefit, and of products used in combination with other treatments. Above all, many OECD countries have expressed concerns about their ability to reconcile access to oncology treatments with spending efficiency and sustainability.

This working paper draws on a series of initial interviews, and an extensive OECD and EU member country survey to attempt to understand the landscape of access and to identify policies and practices deployed by countries to address challenges specific to the provision of access to oncology medicines. These include:

- **Minimising (or even eliminating) patient contributions, and applying fixed co-payments rather than co-insurance**, with safety nets to preserve affordability and avoid catastrophic costs for patients and households.
- **Strengthening the domestic information landscape through routine tracking of use by indication** – this could inform ex-post price adjustments, support the monitoring of expenditures, and contribute to the gathering of “real world” evidence on the performance of these medicines.
- **Improving the design of performance-based managed entry agreements to support the generation and collection of on-market data** – this would require the collection of utilisation and relevant clinical outcome data for products subject to these agreements. Cross-national harmonisation of outcome metrics, as well as data aggregation and information-sharing across payers and countries is highly desirable, particularly for products targeting small populations.
- **Enhancing international collaboration and information sharing to improve countries' collective capacity to address clinical and economic uncertainties** - this could include combining efforts to address evidence gaps through, for example, aggregating routinely collected data at national level or building multi-country registries. This could also include greater collaboration and engagement between pharmaceutical companies, regulators and health technology assessment entities.

Résumé

Les dépenses de médicaments contre le cancer augmentent régulièrement, non seulement en raison du niveau des prix de lancement, mais aussi de l'augmentation du nombre de patients traités (combinaison d'une prévalence croissante, de nouvelles options de traitement, de prolongation de la survie et d'une durée de traitement plus longue). Les progrès thérapeutiques rapides en oncologie et le désir de faciliter un accès rapide à de nouveaux traitements prometteurs créent des défis pour la capacité des pays, y compris les plus riches, à fournir - et à maintenir - un accès aux traitements anticancéreux à un prix abordable. Ces défis sont les suivants : l'incertitude, souvent importante, qui entoure le degré de bénéfice clinique offert par les nouveaux médicaments au moment de l'entrée sur le marché et la décision de prise en charge, ainsi que la complexité de la détermination du prix et de la place, dans la stratégie thérapeutique de produits ayant de multiples indications reflétant des degrés variables de bénéfice clinique et de produits utilisés en combinaison avec d'autres traitements. Surtout, de nombreux pays de l'OCDE ont exprimé des inquiétudes quant à leur capacité à concilier l'accès aux traitements anticancéreux avec l'efficacité et la soutenabilité des dépenses.

Ce document de travail s'appuie sur une série d'entretiens initiaux et une vaste enquête auprès des pays membres pour faire un état des lieux de l'accès aux médicaments anticancéreux et identifier les politiques et pratiques déployées par les pays pour relever les défis spécifiques à l'accès à ces thérapies. Celles-ci incluent:

- **Minimiser (voire éliminer) les contributions des patients, appliquer des copaiements fixes plutôt que des contributions proportionnelles au prix du produit**, et mettre en place des filets de sécurité pour préserver l'accès au médicament et éviter les dépenses catastrophiques pour les patients et les ménages.
- **Renforcer le contexte informationnel national par un suivi systématique de l'utilisation par indication** - ceci pourrait informer les ajustements de prix ex-post, permettre le suivi des dépenses, et contribuer à la collecte de données « en vie réelle » sur la performance de ces médicaments.
- **Améliorer la conception de contrats de performance pour soutenir la production et la collecte de données après la mise sur le marché** - cela nécessiterait la collecte de données sur l'utilisation et sur les résultats cliniques pertinents pour les produits objets de ces accords. L'harmonisation transnationale des mesures de résultats, ainsi que l'agrégation des données et le partage des informations entre les payeurs et les pays sont hautement souhaitables, en particulier pour les produits ciblant de petites populations.
- **Renforcer la collaboration internationale et le partage d'informations afin d'améliorer la capacité collective des pays à faire face aux incertitudes cliniques et économiques** - il pourrait s'agir de combiner les efforts visant à combler les lacunes en matière de données probantes, par exemple en regroupant les données collectées régulièrement au niveau national ou en créant des registres multinationaux. Cela pourrait également inclure une collaboration et un engagement accrus entre les entreprises pharmaceutiques, les agences de régulation et les entités d'évaluation des technologies de la santé.

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List of acronyms and abbreviations

ABPI	Association of the British Pharmaceutical Industry
AIFA	Italian Medicines Agency
ASCO	American Society of Clinical Oncology
ASP	Average sales price
ATC	Anatomical Therapeutic Chemical classification
ATMP	Advanced therapy medicinal products
CADTH	Canadian Agency for Drugs and Technologies in Health
CAR-T	Chimeric antigen receptor T-cell therapy
CDF	Cancer Drugs Fund (England)
CHMP	Committee for Medicinal Products for Human Use
CMS	Centers for Medicare & Medicaid Services (United States)
CTLA-4	Cytotoxic T-lymphocyte-associated protein 4
DDD	Defined daily dose
DHSC	Department of Health & Social Care (England)
DRG	Diagnosis-related group
EBP	Evidence Building Program (Canada)
ECL	European Cancer Leagues
EEA	European Economic Area
EFPIA	European Federation of Pharmaceutical Industries and Associations
EGFR	Epidermal growth factor receptor
EMA	European Medicines Agency
EOPYY	National Organization for the Provision of Health Services (Greece)
ESMO	European Society for Medical Oncology
ESMO-MCBS	European Society for Medical Oncology - Magnitude of Clinical Benefit Scale
EU	European Union
EUnetHTA	European Network for Health Technology Assessment
Euripid	European Integrated Price Information Database
FDA	Food and Drug Administration (United States)
GDP	Gross domestic product
GP	General practitioner

GRADE	Grading of Recommendations Assessment, Development and Evaluation
HAS	Haute Autorité de Santé (France)
HER-2	Human epidermal growth factor receptor 2
HIV	Human immunodeficiency virus
HPRA	Health Products Regulatory Authority (Ireland)
HTA	Health technology assessment
HTAi	Health Technology Assessment International
IBP	Indication-based pricing
INCa	French National Cancer Institute
MEA	Managed entry agreement
MfE	Medicines for Europe
MOH	Ministry of Health
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NoMA	Norwegian Medicines Agency
NTRK	Neurotrophic Tyrosine Receptor Kinase
OOP	Out-of-pocket payments
OS	Overall survival
PBAC	Pharmaceutical Benefits Advisory Committee (Australia)
PBS	Pharmaceutical Benefits Scheme (Australia)
pCODR	pan-Canadian Oncology Drug Review
PD-1	Programmed cell death protein - 1
PD-L1	Programmed cell death ligand - 1
PFS	Progression-free survival
PMPRB	Patented Medicine Prices Review Board
PPRI	Pharmaceutical Pricing and Reimbursement Information network
QALY	Quality-adjusted life-year
RCT	Randomised controlled trial
RWD	Real world data
TKI	Tyrosine kinase inhibitor
TLV	Dental and Pharmaceutical Benefits Agency (Sweden)
WHO	World Health Organization
WH OCC	World Health Organization Collaborating Centre for Drug Statistics Methodology
WHO-EML	World Health Organization 21 st Model List of Essential Medicines
WTP	Willingness to pay

Country abbreviations

AUS	Australia
BEL	Belgium
CAN	Canada
CHE	Switzerland
CHL	Chile
CYP	Cyprus ¹
CZE	Czech Republic
DEU	Germany
DNK	Denmark
EST	Estonia
FRA	France
GBR	United Kingdom (England only)
GRC	Greece
HUN	Hungary
IRL	Ireland
ISR	Israel
ITA	Italy
JPN	Japan
KOR	Korea
LTU	Lithuania
LVA	Latvia
MLT	Malta
NOR	Norway
SWE	Sweden
USA	United States

¹ Note by Turkey: 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. Turkey recognises the Turkish Republic of Northern Cyprus (TRNC). Until a lasting and equitable solution is found within the context of the United Nations, Turkey 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 Turkey. The information in this document relates to the area under the effective control of the Government of the Republic of Cyprus.

Executive Summary

Faced with rapid advancements in oncology treatments, even the wealthiest countries around the globe are increasingly confronting capacity constraints in providing - and sustaining – affordable access to new medicines. This working paper draws on a series of initial interviews, and an extensive OECD and EU member country survey to understand the landscape of **policies and practices deployed by countries to address challenges specific to the provision of access to oncology medicines**.

Among the identified challenges is the often significant **uncertainty surrounding the degree of clinical benefit offered by new medicines** at the time of market entry and coverage determination. In oncology, new products and new indications are increasingly being approved based on evidence from earlier phases of development, on the basis of surrogate endpoint data, or drawing on evidence from non-randomised studies—all of which can lead to overestimation of clinical effectiveness. This is largely driven by the desire to facilitate rapid access to promising therapies in areas of unmet need, but with the result that payers and health technology assessment (HTA) entities may struggle to assess the relative value of these products and make confident decisions on coverage and pricing. Thus far, **a common approach to addressing uncertainty has been the use of managed entry agreements**, mainly with the objective of managing *financial* risks. However, for the most part, these agreements have not helped reduce uncertainties surrounding the clinical benefits of the treatments concerned (and by extension, their cost-effectiveness), though this might be possible with **greater attention to the design of the agreements and more harmonised approaches** across countries.

Another major challenge is that many products have **multiple approved indications, reflecting varying degrees of clinical benefit and therefore, of cost-effectiveness (at a given unitary price)**. This has prompted debate regarding the value of setting different prices by indication, to reflect those differences in cost-effectiveness—a practice known as indication-based pricing (IBP). Among its theoretical advantages is that it can enhance access in circumstances in which coverage would otherwise be denied for indications in which the product is not cost-effective at the unitary price. In practice, however, among those countries that use IBP, few are able to track utilisation by indication to support this practice effectively.

A third major challenge is the **pricing of products used in combination with other treatments**. Frequently, an application for coverage is filed by the sponsor of a new product (the ‘add-on’ therapy), for use in combination with an existing product (the ‘backbone’ therapy). HTA entities assess the value of the combination therapy relative to a comparator (usually the backbone therapy), and payers determine their willingness to pay (WTP) for the combination. Where both products are already marketed in other indications, the aggregate price often exceeds the payer’s WTP, necessitating downward price adjustments for one or both constituent therapies. Ideally, the prices would reflect the respective contributions of the constituent medicines to the overall benefit of treatment, but there is no consensus on how to apportion these shares. In addition, competition law may preclude pricing agreements between companies. Only a few countries have methods for the pricing of combination products, among them France, the United Kingdom (England), and Switzerland, which, after having determined their WTP for a combined therapy, then negotiate with the individual companies. Price adjustments generally take the form of confidential rebates on list prices.

Expenditure on oncology medicines is steadily increasing, not only due to increasing launch prices, but also to growth in the number of patients being treated (a combination of rising prevalence, new treatment options, and increasing duration of treatment). That said, in OECD member countries, retail pharmaceutical expenditure as a proportion of gross domestic product (GDP) has, on average, remained stable over the past decade, at around 1.5%, even though some countries have seen greater growth in

expenditure on medicines administered in hospital or ambulatory care settings. This relative stability in part reflects the implementation of cost containment policies, including the application of overall budget ceilings or expenditure caps. Italy and the United Kingdom (England) have also established dedicated funds for cancer medicines, with caps beyond which companies are required to pay rebates.

A **2019 survey of access to oncology medicines in OECD/EU member countries** was used to compare the approval and coverage status of a sample of 109 product/indication pairs used in five cancer sub-types, and to compute time to access (i.e. time between the date of submission of a marketing authorisation application and the date of coverage decision) for a subset of 31 product/indication pairs approved in the United States since 2014. Information on cost-sharing requirements was also elicited to provide an indication of affordability for patients.

The data clearly show that **access to oncology medicines is unequal across the OECD and EU**. Of the 109 product/indication pairs in the sample, the United States had the largest percentage of product/indications approved and covered (by Medicare), followed by Denmark and Germany (96%, 91%, and 88%, respectively). Chile and Malta had the lowest percentage approved and covered (47% and 46% respectively). While access was more homogeneous for a subset of *essential medicines* (i.e. those included in the WHO 21st *Model List of Essential Medicines* [WHO-EML]), some of the 31 newer product/indication pairs were not yet approved (or launched) in some countries. While differences were also observed in approval and coverage across the five selected cancer sub-types, **all medicines included in the WHO-EML, and at least one in each pharmacological subgroup, were covered in nearly all countries**.

Time to marketing and coverage decisions by public payers for new oncology product/indications varied widely across the OECD/EU. Of the 31 new product/indication pairs approved since 2014, 26 (84%) received their first marketing authorisation in the United States. For individual product/indications, the time between date of first marketing authorisation and coverage decision in a given country ranged from 1 to 66 months, suggesting differences in companies' launch sequences, and in processing times for regulatory, pricing, and coverage decisions.

Inequities in access within countries were also reported, and may be attributable to variations in **coverage** across regions or levels of government, care settings and population groups, as well as to **cost-sharing policies**. While most OECD/EU countries make coverage decisions at the national level, there are exceptions (e.g. Canada, some Nordic countries and United States). In 13 countries, access to self-administered oncology medicines is free of charge, or carries a fixed co-payment. In others, patients are subject to co-insurance (i.e. the patient contribution increases with the price of the medicine). However, almost all countries have 'caps' on user charges, defined in absolute or relative terms (e.g. a fixed amount or proportion of household income – which typically ranges from 1% to 2% of the average wage in European countries, but can exceed 9% and 10% in the United States and Korea respectively).

Although international comparisons can offer useful benchmarks for policy makers, **access must be understood within the context of each country's health care system**. Simple counts of individual medicines approved and covered do not adequately reflect the many factors affecting patient access (e.g. access to providers, levels of cost-sharing, reliability of supply, availability of alternatives etc.).

Drawing on the results of the survey, countries could consider the following **policy options to address the identified challenges in access to oncology medicines**:

- **Minimising (or even eliminating) patient contributions, and applying fixed co-payments rather than co-insurance**, with safety nets to preserve affordability and avoid catastrophic costs for patients and households. Countries that do not require any patient contributions for self-administered oncology medicines or for those administered in outpatient or inpatient hospital settings include the Czech Republic, Lithuania, Malta, Norway and the United Kingdom (England only).

- **Strengthening the domestic information landscape through routine tracking of use by indication** – this could inform ex-post price adjustments, support the monitoring of expenditures, and contribute to the gathering of “real world” evidence on the performance of these medicines. Currently Australia, Belgium, Estonia, France, Hungary, Italy, and Latvia have the ability to track use by indication for some medicines.
- **Improving the design of performance-based managed entry agreements to support the generation and collection of on-market data** – this would require the collection of utilisation and relevant clinical outcome data for products subject to these agreements. Cross-national harmonisation of outcome metrics, as well as data aggregation and information-sharing across payers and countries is highly desirable, particularly for products targeting small populations. Performance-based managed entry agreements are currently used in Australia, Belgium, Estonia, Hungary, Ireland, Israel, Italy, Korea, Lithuania, Latvia, Malta, Norway, Sweden, Switzerland and the United Kingdom (England).
- **Enhancing international collaboration and information sharing to improve countries’ collective capacity to address clinical and economic uncertainties** - this could include combining efforts to address evidence gaps through, for example, aggregating routinely collected data at national level or building multi-country registries. This could also include greater collaboration and engagement between pharmaceutical companies, regulators and HTA entities, with a range of efforts already underway in a number of jurisdictions.

1. Introduction

1. Cancer represents a substantial and growing burden worldwide, in part both a function of the ageing of populations and, in some countries, of improvements in longevity and the success of health care systems. In several countries the lifetime risk of developing some form of cancer exceeds 50% (Tanday, 2015^[1]), and the costs of care, especially of pharmacotherapies, are burgeoning (World Health Organization, 2018^[2]; IQVIA, 2018^[3]). Within the European Union (EU) the cancer burden was estimated to be 3.1 million new cancer cases and 1.4 million cancer deaths in 2018, with direct health costs of EUR 103 billion, of which medications accounted for 31% (Hofmarcher et al., 2019^[4]). In 2015 the US Agency for Healthcare Research and Quality estimated the direct medical costs of cancer care in the United States at over USD 80 billion (Islami et al., 2019^[5]).

2. Recent decades have seen significant advances in cancer survival, stemming from progress in prevention, early detection, pharmacotherapy, and other treatment modalities, but the respective contribution of each is difficult to estimate. Although cancer deaths in Europe increased from 1.2 million in 1995 to 1.4 million in 2018, the rate of increase has been slowing and the death rate has been declining in those under 65 years (Hofmarcher et al., 2019^[4]). Hofmarcher et al. (2019^[4]) estimated that in all European countries, the five-year survival rates increased for most common cancer types between 1995 and 2014. Within this same period, Arnold et al (2019^[6]) found that five-year net survival increased in almost all of seven cancer types in seven high-income countries (Australia, Canada, Denmark, Ireland, New Zealand, Norway and the United Kingdom). The highest observed increases in five-year survival were 16.6 and 21.0 percentage points for colorectal cancer in Denmark in the periods 1995-1999 and 2010-2014, respectively (Arnold et al., 2019^[6]). However, the contribution of oncology medicines to these improvements in survival is challenging to estimate. Moreover, many cancer medicines now considered to be the standard of care have been approved since 2014, and more recent data on five-year survival rates are lacking.

3. The collective understanding of the underlying biology and pathophysiology of many cancers is also driving substantive changes in approaches to care. Increasingly, genomic profiling of tumours is enabling the identification of individual patients or sub-populations more likely to respond to treatment with specific medications. Drug development is progressively targeting particular molecular pathways, in order to identify treatments that can inhibit growth or destroy tumour tissue, while minimising the toxicity associated with conventional chemotherapeutic regimens. Major progress has come with the development of treatments that recruit the body's own immune system to fight some forms of cancer for which there were previously few meaningful treatment options (Page et al., 2014^[7]).

4. These developments have created multiple challenges for countries in achieving and sustaining affordable access to oncology medicines. A series of informal preliminary discussions was undertaken with a subset of countries to try to identify the most pressing issues, the results of which are summarised in Table 1.1. The first issue relates to uncertainty in the assessment of clinical benefit and cost-effectiveness, in part the result of efforts to drive early and rapid approval of novel medications, often based on clinical trials not designed to generate the evidence needed to inform decisions on coverage and payment. A second issue raised was referred to as the “cascade” of indications, a reference to the tendency for oncology medicines to gain marketing approval for multiple indications, often reflecting different degrees of clinical benefit, and thus representing varying levels of cost-effectiveness at a given price. A corollary to this is the challenge of determining the appropriate place in therapy for a new medication, particularly given

the increasing complexity of treatment regimens. The use of multiple medicines with distinct but complementary mechanisms of action, in combination or in close sequence, creates particular challenges both for health technology assessment (HTA) and price negotiation. Not surprisingly, the escalating launch prices and potential budget impact of new oncology medicines, and the concomitant issues of pricing, allocative efficiency, and fiscal risk, were another prominent issue. These create difficulties for payers even in the presence of sound evidence of effectiveness, cost-effectiveness, and identifiable downstream cost offsets. Further to this, differences in coverage policies, purchasing mechanisms, and willingness to pay (WTP) can create inequities in access and lead to 'postcode prescribing'. Finally, all of the preceding issues contribute to the challenge of meeting patient expectations of timely access to new oncology medicines.

Table 1.1. Summary of challenges identified in managing access to oncology medicines

Key Issues	Elements	Description
Uncertainty in the assessment of clinical benefit, cost-effectiveness and budget impact	<ul style="list-style-type: none"> • Early/rapid approval with immature/paucity of data • Clinical trials not designed to address key issues for HTA/payers • Use of surrogate endpoints of uncertain validity leading to uncertainty in clinical benefit • Pan-tumour indications • Transition from acute to chronic treatment 	The nature and level of evidence presented to/accepted by regulatory agencies to support marketing approval create uncertainties in estimating the extent of clinical benefit for HTA entities/payers, with flow on to cost-effectiveness, and even budget impact. This may prompt the use of MEAs and real world data collection to attempt to overcome these uncertainties.
Cascade of indications	<ul style="list-style-type: none"> • Multiple indications in populations of varying size 	Multiple indications for a given medication reflecting differences in degrees of benefit, and varying levels of cost-effectiveness at a given price.
Place in therapy ¹ and pricing of combination regimens	<ul style="list-style-type: none"> • Increasing use of combination therapies and complex treatment regimens 	Increasing use of multiple medicines with distinct but complementary mechanisms of action in combination or close sequence creates challenges for HTA and pricing.
Increasing up-front costs, reduced affordability and sustainability	<ul style="list-style-type: none"> • Rapidly increasing launch prices • Challenge of upfront payment especially if pent-up demand, delayed benefits 	Escalating launch prices have been widely documented. These create difficulties for payers even in the presence of sound evidence of effectiveness, cost-effectiveness, and downstream cost offsets.
Inequity in access	<ul style="list-style-type: none"> • Coverage and access (and societal willingness to pay) may vary at national, regional and institutional level ('postcode prescribing') 	Differences in willingness and capacity to pay across countries, regions and even institutions, leads to inequities in access.
Meeting patient expectations	<ul style="list-style-type: none"> • Rapid approval of multiple new therapies 	Patient expectations of timely access not being met; challenges for HTA/ payers in assimilating rapid entry of multiple new treatments.

Note: HTA health technology assessment, MEA managed entry agreement. 1. Place in therapy refers to whether a medicine is to be used by itself or in combination, in which line of treatment, or in which sequence of treatment for a given stage of disease etc.

Source: Authors, based on preliminary interviews for 2019 OECD survey on challenges in access to oncology medicines.

5. This working paper draws extensively on information from a three-part survey of OECD member countries and EU Member States distributed in September 2019, to which a total of 25 countries² responded (see Annex A, Table A A.1; further details of the survey and its components are also provided in Annex A). Chapter 2 describes the different approaches taken by countries in attempting to address some of the challenges discussed above, including uncertainty in assessment of clinical benefit; the cascade of indications; place in therapy and pricing combination regimens; and increasing costs within budget constraints. Chapter 3 presents data from OECD/EU countries on the existing state of access based on a defined sample of oncology medicines, and explores some of the challenges associated with access, cost-sharing, and meeting patient expectations.

² Australia, Belgium, Canada, Chile, Cyprus, the Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Japan, Korea, Latvia, Lithuania, Malta, Norway, Sweden, Switzerland, the United Kingdom (England only), and the United States.

2. Country approaches to managing access to oncology medicines

6. From a series of preliminary interviews, a number of issues of common concern were identified, which were either specific to oncology medicines, or considered particularly challenging in this therapeutic area. Drawing on 24 country responses to Part 1 of the OECD survey³, this section describes these challenges and the approaches being applied by these countries in attempting to address them. Sections successively address the challenges of mitigating uncertainty in the assessment of clinical benefits (2.1); managing the cascade of indications (2.2); managing place in therapy and pricing of combination products (2.3); and lastly managing increasing treatment costs within budget constraints (2.4).

2.1. Mitigating increasing uncertainty in the assessment of clinical benefit

7. In all therapeutic classes, a mismatch has been observed between the nature and level of evidence required and accepted by regulatory agencies to support marketing authorisation, and that desired by health technology assessment (HTA) entities and payers to make evidence-informed coverage decisions.

8. Regulatory agencies are required to assess safety, quality, and efficacy and to establish that in the population targeted, the benefits of a drug outweigh the risks associated with its use. They evaluate the data from clinical trials submitted for regulatory approval, trials that are often limited to subjects from narrowly-defined populations (i.e. generally excluding the very old, very young and very sick), thus limiting the generalisability of the results. Frequently, these trials measure or report *efficacy* results using surrogate endpoints⁴ or biomarkers rather than clinical endpoints (Johnson, Williams and Pazdur, 2003^[8]; Kim and Prasad, 2015^[9]; Kim and Prasad, 2016^[10]). The trials do not always involve an active comparator (though active comparators are more common in oncology than in other therapeutic areas). They may not measure or report changes in health-related quality of life.

9. By contrast, HTA entities assess comparative or relative effectiveness, as well as incremental cost-effectiveness or value for money, and for which evidence from clinical trials used for regulatory purposes is not generally adequate. Key questions for HTA include *how does the new medicine compare with the existing standard of care?* and *how will it perform in the wider population?* In the absence of regulatory trial designs more suited to generating evidence for HTA there may be considerable residual uncertainty around the comparative value of a new therapy. Products for which the clinical benefits and target

³ Australia, Belgium, Canada, Chile, Cyprus, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Japan, Korea, Latvia, Lithuania, Malta, Norway, Sweden, Switzerland, the United Kingdom (England only), the United States

⁴ A surrogate endpoint is an indirect measure of the effect of a specific treatment that is expected to predict a final clinical outcome of interest such as overall survival and/or quality of life (Kemp and Prasad, 2017^[95]). A surrogate endpoint may be considered to be valid if it is in the causal pathway of the disease process and is correlated with the clinical endpoint in such a way that the change in the surrogate fully captures the net effect of the intervention on the final clinical endpoint (Fleming, 2005^[96]). The use of surrogate endpoints is often favoured when the measurement of more patient relevant or final clinical endpoints would be difficult or invasive, or would require larger and longer trials. However, not all surrogate endpoints used in clinical trials are well validated.

population are uncertain will be associated with concomitant uncertainty in both cost-effectiveness and expected utilisation, and by extension, in budget impact.

2.1.1. In oncology, uncertainty surrounding clinical benefit can be considerable

10. In oncology, this mismatch is worsened by the fact that medicines are often approved via expedited or 'fast-track' processes that often rely on surrogate endpoint or biomarker data rather than final, clinical outcomes. While these expedited processes are intended to accelerate patient access to promising treatments, post-marketing studies are frequently needed to confirm evidence of clinical benefit. There are many sound reasons for using surrogate endpoints: endpoints measured soon after the intervention of interest are less prone to 'contamination' by other factors (such as co-interventions, or death from unrelated causes) before the clinical endpoint of interest is reached; measurement of a final, clinical outcome may be excessively invasive or expose patients to excessive risk; and patient survival may require lengthy follow-up and/or large numbers of patients to render concrete evidence of benefit, particularly in early disease.

11. The surrogate endpoints used, however, have not always been well validated, so that the extent to which a change in the surrogate predicts the extent of change in the more clinically relevant endpoint may not always be clear. For example, in 2018, a systematic review found that there was no significant association between the frequently used surrogate endpoint of progression-free survival (PFS) and measurements of quality of life in cancer trials (Kovic et al., 2018^[11]). A 2019 systematic review of trial meta-analyses found low or only modest correlation between several of the surrogate endpoints commonly used in oncology trials and overall survival (OS) (Haslam et al., 2019^[12]). Correlation between surrogate endpoints and OS may be better in some settings than in others. In 2018, a large-scale meta-analysis provided an overview of the current evidence of surrogate endpoints for OS in randomised controlled trials (RCTs) across a range of cancer types and settings. The authors found that disease-free survival has adequate surrogate properties for OS in adjuvant treatment for non-small-cell lung cancer, gastric cancer, head and neck cancer, and colon cancer. In advanced settings, the study found that progression-free survival may be appropriate for metastatic colorectal cancer, lung cancer, and head and neck cancer (Savina et al., 2018^[13]). However, uncertainty in the interpretation of results may also be exacerbated in trials designed to allow participants to cross over to another therapy once a favourable result is recorded against the surrogate endpoint. While there will often be sound ethical and scientific reasons for permitting crossover within such trial, this can nevertheless introduce additional complexity in the interpretation of the data and can undermine attempts to clarify or confirm the validity of the surrogate marker.

12. The confirmation of benefits through post-marketing studies is thus important for policy makers. Two studies, looking at cancer indications approved by the US Food and Drug Administration (FDA) and through the European Medicines Agency (EMA) provide some insights into post-market benefit assessment. The most recent and complete study, from May 2018, reviewed information from post-marketing studies for 93 cancer product/indications that received accelerated approval from the US FDA between December 1992 and May 2017. Clinical benefit was confirmed for two-thirds of the indications (58), measured on clinical outcomes such as OS for 20%, and on surrogate endpoints for 41%. Benefit was not confirmed in 9%, and post-marketing studies were ongoing for 10% of the sample, pending for 11%, and delayed for 5% (Gyawali, Hey and Kesselheim, 2019^[14]). Another study looked at evidence available for the 68 cancer product/indications approved by the EMA between 2009 and 2013. At the time of approval, significant improvement in survival was demonstrated for 24 (35%) of these product/indications, and improvement in quality of life in 7 (10%). For the remaining 44 product/indications, post-marketing studies provided evidence of life extension for 3 (7%), and of improvement in quality of life for 5 (11%). The authors concluded that pre- and post-market evidence available for these 68 product/indications showed improvement in survival or quality of life for 51%, while the benefits remained uncertain for the remaining 49% (Davis et al., 2017^[15]).

13. Particularly challenging in this respect are ‘pan-tumour’ products,⁵ that are mutation- rather than organ- or tissue-targeted, as it may be unclear how, and in whom they will be used and effective (see Box 2.1). While recent approvals by several regulatory agencies of cancer treatments based solely on the presence of a genetic feature in a solid tumour, rather than the site, tissue or cancer type, are an important advance in cancer management informed by tumour-specific genetic profiles, it remains the case that responses will be heterogeneous (and still measured on surrogate endpoints). For example, although patients with certain cancer types (e.g. lung cancer and melanoma) typically have good responses to immune checkpoint inhibitors such as pembrolizumab (Keytruda®), not every patient responds to the same extent to the treatment. One particular challenge encountered in the value assessment of products with pan-tumour indications may be the choice of an appropriate comparator. These products are often evaluated in “basket” trials, in which a targeted therapy is evaluated for multiple diseases that have common molecular alterations, and which are often single-arm studies (Park et al., 2019^[16]). More traditional, disease-specific, follow-up studies may ultimately be needed to inform both clinical protocols and HTA (Tao, Schram and Hyman, 2017^[17]).

14. While the gold standard of evidence is clinical endpoint data (e.g. OS) from RCTs, these trials may be neither feasible nor ethical, and regulatory decisions may be made with less robust evidence. The challenges of undertaking RCTs in oncology may include a limited understanding of the natural history and epidemiology of rare tumours; the absence of standard companion diagnostic tests; difficulties in subject accrual (e.g. in rare tumour types); and population heterogeneity; as well as the inherent difficulty in interpreting outcomes measured using surrogate endpoints of uncertain validity. More broadly, the growing trend within regulatory agencies to accept single-arm studies as the basis for expedited approval not only weakens the evidence base for any subsequent comparative assessment, but, by definition these studies cannot be used to generate comparative evidence of the progression of the cancer in the absence of the new medicine, (though in some cases comparisons can be made using historical controls). Importantly, any additional evidence generated for drugs approved on the basis of non-randomised studies must be considered in the knowledge that important biases cannot be excluded. Gyawali et al (2020^[18]) assessed the response rate and durations of response measured in non-randomised versus randomised controlled trials for a sample of 19 oncology product/indication pairs approved by the FDA on the basis of changes in biomarkers. Response rates did not differ significantly between the two types of trials (pooled ratio 1.06 with 95% Confidence Interval of 0.95-1.20), but duration of response was significantly higher in the non-randomised studies (pooled ratio 1.17 with 95% Confidence Interval 1.03-1.33). The authors concluded that the effects of drugs approved on the basis of duration of response in non-randomised trials may be overestimated, and a poor proxy for OS (Gyawali et al., 2020^[18]).

15. Another layer of uncertainty is associated with the short duration of clinical trials for the introduction of advanced therapy medicinal products (ATMP), such as Chimeric antigen receptor T-cell therapy (CAR-T). From a payer point of view and for price setting, it is unclear whether these treatments are in fact ‘one-off’ or whether re-treatment will be required, which adds uncertainty in estimates of clinical benefit, cost-effectiveness and budget impact. Residual uncertainty regarding the extent and duration of benefit from treatment also arises from the transition of some drugs from acute or episodic treatment to chronic therapy (e.g. trastuzumab emtansine - Kadcyla®).

⁵ These are medicines that are approved on the basis of targeting specific mutations or genomic alterations in different tumours, also known as “tumour-agnostic” or “histology-independent” therapies, because they target the genomic alteration within a tumour, regardless of where in the body it has formed.

Box 2.1. Medicines approved with pan-tumour indications

Note: A pan-tumour approval may be an additional indication for a product already approved for use in multiple indications. The pan-tumour indication does not necessarily overlap with existing indications.

Source: Authors based on definition of pan-tumour indications.

Examples of medicines recently approved:

US Food & Drug Administration (May 2017)

Keytruda® (pembrolizumab) is indicated for the treatment of adult and paediatric patients with unresectable or metastatic solid tumours that have been identified as having a biomarker referred to as microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR). This indication covers patients with solid tumours that have progressed following prior treatment and who have no satisfactory alternative treatment options and patients with colorectal cancer that has progressed following treatment with certain chemotherapy drugs.

Note that this is an additional indication for pembrolizumab and does not replace existing indications.

European Medicines Agency (July 2019)

Vitrakvi® (larotrectinib) as monotherapy is indicated for the treatment of adult and paediatric patients with solid tumours that display a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have no satisfactory treatment options.

Note that this is the initial marketing authorisation for larotrectinib, although it had previous orphan designations in the treatment of soft tissue sarcoma, salivary gland cancer, glioma, and papillary thyroid cancer.

Japanese Pharmaceuticals and Medical Devices Agency (June 2019)

Rozlytrek® (entrectinib) is indicated for the treatment of adult and paediatric patients with NTRK fusion-positive, advanced/recurrent solid tumours. This is the initial marketing authorisation for entrectinib in Japan.

Source: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-cancer-treatment-any-solid-tumor-specific-genetic-feature> ; <https://www.ema.europa.eu/en/news/first-histology-independent-treatment-solid-tumours-specific-gene-mutation>; <https://www.pmda.go.jp/files/000232794.pdf>, consulted on 18 March 2020.

2.1.2. Countries have so far focused on limiting the financial risks associated with uncertainty

16. Sixteen⁶ respondents to the survey (67%) confirmed that the issue of “high uncertainty” had been flagged in their countries, either in individual assessment reports or in other documents, and almost all respondents had in place mechanisms to mitigate uncertainty in coverage and/or pricing decisions.

17. The OECD survey mainly explored policy responses from HTA entities and payers and did not specifically address the role of regulatory agencies. The latter can, however, play a key role in reducing the gap between evidence available at the time of marketing authorisation and that needed for both payer and clinical decision making. Some regulatory agencies and HTA bodies now offer opportunities of ‘early dialogue’ with companies to help them develop clinical trial programmes that are more responsive to the needs of both payers and regulators. To address the issue of lack of representativeness of subjects in clinical trials, the US FDA recently published an industry guidance document on the inclusion of older adults in cancer clinical trials.⁷ In Ireland for example, the Health Products Regulatory Authority (HPRA) provides scientific advice to pharmaceutical companies, both nationally and at EU level and actively contributes to the work of the scientific advice working party at the European Medicines Agency. The HPRA has met with the Irish HTA body and the National Centre for Pharmacoeconomics on a number of occasions and participated in relative effectiveness assessment of pharmaceuticals at EU level. Since 2010, pharmaceutical companies can receive parallel scientific advice from both EU regulators and HTA entities concerning their clinical development plans. Tafuri et al. (2018^[19]) investigated the uptake of such advice on two key aspects of medicine development relevant to both regulators and HTA entities: clinical endpoints and choice of control/comparator. All included studies that received advice between 2010 and 2015 implemented endpoints that met the needs of both regulators and at least one HTA entity, while just over half used comparators that satisfied both regulators and at least one HTA entity (Tafuri et al., 2018^[19]).

18. A few countries have addressed the question of uncertainty in recent updates to their guidelines for evaluation and/or priority setting. For example, France’s *Haute Autorité de Santé* (HAS) updated its principles of assessment in 2018, specifying the circumstances in which clinical benefit may be determined despite a high degree of uncertainty, being: severe disease; unmet medical need; where initial data suggest benefits to patients; and where there is a development plan to reduce uncertainty in the short term, through further clinical trials or use of real-world data (HAS, 2018^[20]). In the United Kingdom, the National Institute for Health & Care Excellence (NICE) has been invited to provide guidance in its assessments on how to manage the types of uncertainty most influential in cost-effectiveness studies (Department of Health and Social Care and ABPI, 2018^[21]). However, to our knowledge, these recommendations have not yet been published. In Norway, the recent white paper *Principles for Priority Setting in Health Care* stipulates that a high level of uncertainty in the assessment of benefit must in principle lead to a lower level of priority (i.e. a lower cost-effectiveness threshold) (Norwegian Ministry of Health and Care Services, 2017^[22]). However, the document also calls for the application of less stringent requirements when assessing interventions targeted to small patient groups. A higher cost-effectiveness threshold may be accepted for medicines targeting very small patient groups with an extremely severe condition. The Norwegian Medicines Agency (NoMA) has also published guidelines to define those medicines eligible for this analytic framework: they must target a very small patient group (global prevalence of less than 1/100,000 and less than 50 patients in Norway); they must be for the treatment of an extremely severe condition (absolute loss of 30 quality-adjusted life years [QALYs] in the absence of treatment); and the expected benefit must be substantial (i.e. at least 2 QALYs gained in comparison with standard treatment) (NoMA, 2018^[23]).

⁶ Australia, Belgium, Canada, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Israel, Norway, Sweden, Switzerland, the United Kingdom (England only), the United States.

⁷ See <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/inclusion-older-adults-cancer-clinical-trials>, consulted on 12 March 2020

19. Respondents were asked what policies and/or approaches, if any, they used to address uncertainty in coverage and/or pricing decisions, and 21 of 24 reported utilising financial and/or performance-based managed entry agreements (MEAs) (see Figure 2.1). A recent OECD report on country experiences with MEAs (Wenzl and Chapman, 2019^[24]) found that oncology medicines are often the subject of such agreements. In general, most of the agreements are financial in nature and aim to keep actual prices paid confidential, or to mitigate risks to budget impact (e.g. price-volume agreements). The report also notes that to date, performance-based agreements have not always been effective in elucidating the performance of products in real world settings.

20. Eight countries reported utilising post-marketing studies to address uncertainty at the time of marketing approval (see Figure 2.1). This is the case for medicines funded through the ‘new’ Cancer Drugs Fund (CDF) in England⁸, for example. Under this scheme, Managed Access Agreements rely heavily on post-marketing studies requested by the EMA for the generation of evidence to address uncertainties (Wenzl and Chapman, 2019^[24])

21. ‘Real world data’ (RWD)—data collected in routine clinical practice—can also be used to address some of the uncertainties inherent in assessments of efficacy, safety, comparative effectiveness and cost-effectiveness. Ten countries use clinical registry data in this way (see Figure 2.1). In Italy, for example, nation-wide web-based registries have been created for each product/indication or line of treatment. While the principal aim of the Italian Medicines Agency (AIFA) is to monitor the appropriate use of the medicines in clinical practice and the application of the financial terms of MEAs, the data are also useful in addressing some uncertainties, for example, concerning the length of treatment, or duration of effect (Montilla et al., 2015^[25]). Moreover, Italy has implemented a pricing policy which assigns medicines to one of three different categories according to the perceived level of innovation they represent (innovative, potentially innovative, not innovative), based on an evaluation that takes into account clinical need, added therapeutic value, and quality of evidence (using the Grading of Recommendations Assessment, Development and Evaluation [GRADE] criteria). France has a National Health Data System (*Système National des Données de Santé* (SNDS)) which collates and analyses data from the principal public health databases in France. Within this framework, the SNDS is able to partially monitor the consumption of certain anti-cancer medicines, in particular from cancer registries⁹. In Greece, the national health insurance fund maintains a registry for multiple myeloma, while Hungary has registries for high cost oncology medicines.

22. Six countries reported relying on routinely-collected data to reduce uncertainty surrounding the clinical benefits of new products (see Figure 2.1). Australia, for example, uses routinely-collected data to manage financial MEAs, and uses a range of data sources to reduce uncertainty surrounding the comparative effectiveness of new products in performance-based MEAs. In Germany, recent legislation allows the HTA entity to ask a pharmaceutical company to collect data from clinical practice for the purposes of the benefit assessment. This is, however, limited to orphan medicines and medicines with conditional or exceptional approval, as these products often receive market authorisation with less data from clinical trials. In Canada, a number of payers have introduced initiatives to collect RWD. Cancer Care Ontario, for example, runs an Evidence Building Program (EBP) through which patients can gain access to existing medicines for use in indications not yet accepted for routine funding because of a high degree of uncertainty. Medicines are only eligible for this programme if they fulfil a number of conditions, two in particular: that the collection and analysis of the real-world data are expected to be sufficient to inform a future funding decision, and that there are no studies already underway that are expected to address the issue within the EBP funding period.¹⁰

⁸ See <https://www.england.nhs.uk/cancer/cdf/>, consulted on 18 March 2020.

⁹ See <https://www.snds.gouv.fr/SNDS/Accueil>, consulted on 31 August 2020.

¹⁰ See https://www.cancercareontario.ca/en/Funding/Evidence_Building_Program, consulted on 18 March 2020.

23. Switzerland reported that post-marketing studies, collation of routinely-collected data, and registries may be required for temporary coverage. In Japan, HTA may be used *after* initial coverage and pricing decisions for medicines with high budget impact, in order to adjust prices according to the cost-effectiveness of the product/indication.

Figure 2.1. Policies and approaches to address uncertainty in coverage and/or pricing decisions across OECD/EU countries

Based on responses from 24 countries to the OECD survey (multiple options possible per country).

Note: MEA managed entry agreement

In Cyprus, formal MEAs do not exist but the Ministry's procurement unit can negotiate discounts.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

24. All responding countries reported that they would see value in international collaboration or information sharing to address clinical and/or economic uncertainties, albeit with some caveats. Recognising that many of the issues faced during the medicine review process were common across similar systems, respondents saw value in understanding different approaches to these issues as well as combining efforts. Several countries mentioned existing collaborative initiatives such as BeNeLuxA, Health Technology Assessment International (HTAi), the European Network for Health Technology Assessment (EUnetHTA), FINOSE, the Valletta Declaration, the European Integrated Price Information Database (Euripid) and the Pharmaceutical Pricing Reimbursement Information (PPRI) network (see Box 2.2 for brief descriptions of these initiatives). To improve their collective capacity to address uncertainty, countries also suggested they could consider: aggregating national routinely-collected data sources or building multi-country registries, especially for orphan medicines; developing a global approach to performance-based managed entry agreements; harmonising approaches to the assessment of clinical and economic outcomes (including at the regulatory level¹¹); and joint efforts to address evidence gaps (e.g. harmonised requirements for post-marketing studies or other types of evidence generation). However, some concerns were flagged regarding the feasibility of information sharing and the generalisability of national data across health care systems and populations.

¹¹ For example, this could include harmonised requirements for robust comparative studies, as well as for relative effectiveness assessments by HTA entities (e.g. through the EUnetHTA initiative, see Box 2.2).

Box 2.2. Existing international collaboration initiatives

BeneluxA: Five countries (Belgium, the Netherlands, Luxembourg, Austria and Ireland) contribute to this initiative, whose aim is to improve access to “ensure sustainable access to innovative medicine at affordable cost for [...] patients” and have agreed to cooperate in the following activities: horizon scanning, information sharing and policy exchange; HTA (with EUnetHTA). Technical experts have been collaborating to produce HTA reports; as well as a common template for submission of a dossier. See: <https://beneluxa.org/>

European Network for Health Technology Assessment (EUnetHTA) aims to “contribute to a sustainable model for the scientific and technical cooperation on HTA in Europe in close collaboration with the stakeholders and the European Commission”. It comprises 80 organisations from 30 countries. Key objectives include early dialogues with manufacturers, joint HTA reports, and post launch evidence generation. See: <https://eunetha.eu/>

Euripid collaboration is a “voluntary and strictly non-profit cooperation between mostly European countries on building up and maintaining a database with information on national prices and pricing regulations of medicinal products in a standardized format”. The online database, which contains data on official prices of publicly reimbursed medicines, is not publicly accessible. See: <https://www.euripid.eu/aboutus>

Health Technology Assessment International (HTAi) is a global non-profit, scientific and professional society for all those who produce, use or encounter health technology assessment. They represent over 80 organisations and 2 500 individual members from 65 countries worldwide. Members include “researchers, policy makers, industry, academia, health service providers, agencies and patients”. See: <https://htai.org/about-htai/>

The International Horizon Scanning Initiative (IHIS) was launched in 2018 to organise a formal cooperation around horizon scanning between countries willing to become members of this initiative <https://ihis-health.org/>.

The Pharmaceutical Pricing and Reimbursement Information (PPRI) Network is an informal network of experts involved in pharmaceutical policy from 47 countries, mostly but not only European. Members of this network meet twice a year to exchange information on challenges and policy responses <https://ppri.goeg.at/>

Valletta Declaration: The Valletta Declaration was signed on 8th May 2017. This regional cooperation scheme now includes the Ministries of Health of Cyprus, Croatia, Greece, Ireland, Italy, Malta, Portugal, Romania, Slovenia, and Spain, covering 160 million citizens, representing 32% of the total EU population. According with the Declaration, the Valletta Technical Committee was established. The Committee aims to explore new areas of activity, such as mechanisms for joint negotiation and procurement as well as information and best practice sharing.

In 2020, The World Health Organization’s Regional Office for Europe published a report assessing five cross-country collaborations to improve access to medicines and vaccines in the region: the **Baltic Procurement Initiative**, BeneluxA Initiative, **Fair and Affordable Pricing**, **Nordic Pharmaceutical Forum** and Valletta Declaration. See: <https://www.euro.who.int/en/publications/abstracts/cross-country-collaborations-to-improve-access-to-medicines-and-vaccines-in-the-who-european-region-2020>

Source: Authors as above, consulted March 2020, updated September 2020.

2.2. Managing the ‘cascade’ of indications

25. Globally, between 2013 and 2017, 45 new oncology drugs entered the market, many of them approved for multiple indications or for use within a combination therapy regimen. The number of approved product/indications increased by 40% during this period, with an average of five indications per new active substance. In 2018, 75% of targeted therapies were used in multiple indications, and checkpoint inhibitors were approved for 10 indications (IQVIA, 2018^[3]).

26. Beyond the targeted disease itself (e.g. tumour type, cancer site, genetic mutation), an approved indication or formulary listing may also specify disease severity, patient status, line of treatment (e.g. first line, second line), or use within a combined treatment regimen. New indications may be added over time and others may also evolve. For example, a treatment initially approved or covered only in second line therapy may move to first line as evidence accumulates.

27. The following sections discuss issues in the pricing of medicines used across multiple indications, as well as the management of the use of these medicines outside their covered indications.

2.2.1. Pricing products with multiple indications is challenging

28. For products with multiple approved indications, the degree of clinical benefit may vary significantly between indications, and as a result so will the cost-effectiveness (at a given price); this creates a substantial challenge both for companies in setting a price acceptable to payers, and for payers in seeking to ensure acceptable cost-effectiveness. Pricing and coverage decisions are also particularly challenging when multiple indications, or extensions of indications, for a given product are approved successively. Some oncology products may be approved for several indications with small populations. Some recent examples include nivolumab (Opdivo®) and pembrolizumab (Keytruda®), which have orphan designations in the United States for 6 and 10 indications respectively.^{12,13}

29. In the literature, indication-based pricing (IBP)—also known as indication-specific pricing—refers to where the price paid for a medicine is determined according to its perceived value in each indication. IBP has been described as a way of ensuring both static and dynamic efficiency. It is expected to improve access in those indications in which use of a drug would not be cost-effective (and thus not covered) if the drug was priced at a level reflecting its value in the most cost-effective indication. At the same time, it is also expected to encourage investment in research and development supporting the use of drugs in follow-on indications of potentially smaller incremental benefit, and which would be unlikely to be developed if there were a risk of a coverage denial, or of a price reduction not fully compensated by an increase in volume (Neri, Towse and Garau, 2018^[26]). There is, however, no consensus definition IBP (Cole, Towse and Zamora, 2019^[27]; Bach, 2014^[28]; Campillo-Artero et al., 2019^[29]). The broader concept of IBP can include: a) discrete branding of products in different indications; b) different prices charged at the point of sale; c) different prices applied ex-post through managed entry agreements or rebates; and d) a blended price based on a population-weighted average value across indication. Options b) and c), however, depend on payers’ ability to track both utilisation and the indications for which the drugs are prescribed, which in many countries may not be achievable within current data management infrastructures and information systems. If tracking utilisation were to be implemented solely for payment purposes (rather than for other sound policy reasons such as promoting rational use and good prescribing), there is likely to be a trade-off between the benefits of this monitoring and the administrative overhead for the entity (company or payer) bearing the cost of data collection.

¹² See <https://www.accessdata.fda.gov/scripts/opdlisting/ood/>, accessed 10 February 2020.

¹³ Note that due to differences in orphan drug criteria, these medicines do not have orphan designation in Europe.

30. Fifteen¹⁴ of the 24 countries (63%) who responded to the survey reported that the issue of the cascade of indications had been given particular attention in that country. Responding countries were categorised according to their willingness to take into account differential values when pricing multi-indication products, as well as their capacity to track use by indication in their systems (see Table 2.1).

31. The majority of respondents reported unitary prices for products with multiple indications, irrespective of varying benefit and value (see bottom, right-hand, grey cell of Table 2.1). To be covered in Norway and the United Kingdom (England), a product must be cost-effective at the price proposed across *all* indications. One third of responding countries (8 out of 23) reported setting different prices across indications according to value. Australia and Germany described calculating a blended or 'shadow' price based on the weighted average price per indication in the anticipated treatment populations. Italy, Belgium, France and Switzerland negotiate prices per indication but use a single list price, with ex-post confidential rebates. In Italy, where use is tracked through cancer registries, ex-post rebates can be based on actual use in each indication. In France, use by indication can only be tracked for new products paid for outside Diagnosis Related Group (DRG) payments to hospitals, as hospitals must claim reimbursement by indication for these products. In Belgium, the capacity to track use by indication is limited, while in Switzerland tracking use by indication is not currently possible. Finally, Estonia and Latvia are able to apply differential prices per indication ex-ante.

Table 2.1. Pricing products with multiple indications in OECD/EU countries

Pricing mechanism	Ability to track use by indication	No ability to track use by indication
Differential prices per indication applied ex-ante e.g. simple financial discounts at the point of sales according to intended usage	Estonia, Latvia	
Differential prices per indication applied ex-post through rebates	Belgium ¹ , France ¹ , Italy	Belgium ¹ , France ¹ , Switzerland
Blended / single weighted price		Australia ² , Germany
Single price – ie not taking into account different values of multiple indications	Hungary ³	Canada, Chile, Cyprus, Denmark, Greece, Ireland, Israel, Japan, Korea, Lithuania, Malta, Norway ⁴ , Sweden ⁴ , United Kingdom ⁴

Note: 1. In Belgium and France, tracking use by indication is only possible for some product/indications but not for all. 2. Where medicines are subject to specific indication-based access criteria when listed on the Pharmaceutical Benefits Scheme (PBS), the usage can be tracked based on the (PBS). 3. In Hungary, usage of products can be tracked by indication in most cases. 4. In Norway, Sweden and the United Kingdom (England), the price of the product is unique but based on the fact that the medicine should be cost-effective in all indications (and not on a weighted average of value-based prices per indication).

Source: Authors' synthesis based on 2019 OECD survey on challenges in access to oncology medicines.

32. In order to clarify payers' willingness to consider value when regulating pharmaceutical prices, countries were asked to report the effect, if any, on an existing product's price of the addition of a new indication. The responses are shown in Table 2.2.

¹⁴ Australia, Belgium, Canada, Denmark, France, Hungary, Ireland, Israel, Italy, Japan, Malta, Norway, Sweden, Switzerland, and the United Kingdom (England only).

Table 2.2. Price change likely to occur following approval and coverage of a new indication of an existing product in OECD/EU countries

What is likely to happen when a new indication is added for a product already covered?	Country
Product price likely to remain unchanged, no reference to value or population per indication	Canada (max. price set at Federal level) ¹ , Cyprus, Israel, Lithuania, Malta, Sweden
Product price likely to be reduced to account for increase in volume / market expansion / budget impact	Chile, Belgium, Denmark (company's decision), France, Israel, Italy, Japan (if large volume increase), Korea, Latvia, Lithuania, Malta, Sweden, Switzerland
List product price remains unchanged, but new or existing MEA may be (re)negotiated (e.g. simple discount, price-volume agreement, etc.)	Australia, Belgium, Denmark (volume-based discounts), France, Greece (volume rebates), Hungary (volume-based), Italy, Latvia, Switzerland
Product price might need to be reduced if new indication is less cost-effective than existing ones	Norway, United Kingdom (England, with possible MEA if this would cause a net loss in revenue)
Price might change to reflect value and volume per indication	Australia, Belgium ² , Estonia, Germany, Ireland, Switzerland

Note: MEA managed entry agreement.

Multiple options possible per country.

1. In Canada, third-party payers (private insurers and public plans) are free to negotiate prices below the maximum price established at the national level. 2. This is not the most common situation in Belgium.

Source: Authors' synthesis based on 2019 OECD survey on challenges in access to oncology medicines.

33. In some countries the unit price of a product may be reduced to offset increases in sales volumes. Thirteen countries reported that a medicine's price was likely to be reduced in response to an increase in volume, although in Denmark this would generally be at the discretion of the manufacturer. In nine countries, the *list price* of the product is likely to remain unchanged but new (or existing) product-specific agreements (formal managed entry agreements or other contractual arrangements) may be (re)negotiated. Both Norway and the United Kingdom (England) reported prices might need to be reduced to ensure that a product remains cost-effective across all indications. This could potentially deter companies from applying for coverage of less cost-effective indications if it could lead to a net loss of revenue, but the framework agreement signed between the England National Health Service (NHS) and the pharmaceutical industry stipulates that a managed entry agreement can be signed to avert such situations (see art. 3.36 in (Department of Health and Social Care and ABPI, 2018^[21])).

34. In the United States, medicines covered under Medicare Part B (those administered as part of a physician service) are reimbursed to providers at 106% of the average sales price (ASP) of the product.¹⁵ The approval of a new indication would not directly lead to a variation in the reimbursement amount, however sales of the product in a new indication could potentially impact the ASP if other payers renegotiated their prices. For medicines covered under Part D (medicines self-administered in primary and ambulatory care), prices are negotiated by private Part D plans; it is therefore not possible to determine the impact of a new indication, if any, on prices¹⁶.

¹⁵ The ASP reflects the average price, net of all price concessions (such as discounts and rebates), for all sales of the product in the U.S. market (with limited exceptions), for any indication.

¹⁶ Note that the US now allows indication -based formulary design in Medicare Part D.

2.2.2. “Off-label” and “off-coverage” use may be covered in some circumstances

35. The use of medicines outside the indications approved by the regulator (*‘off-label use’*) is very common in oncology. As a therapeutic area of high unmet need, prescribers and patients are often willing to accept the use of medicines in circumstances in which their efficacy and safety profiles have not yet been clearly established. A systematic review of the literature showed that off-label use of oncology medicines was in the range of 18% to 41% for hospitalised patients and 7% to 50% in ambulatory care. In total, between 13% and 71% of adult oncology patients received at least one off-label chemotherapy during their course of treatment, and this was more common where patients had exhausted all standard lines of treatment. The main reasons for off-label use were use in an unauthorised indication for a specific tumour and use in an unauthorised line of treatment (Saiyed, Ong and Chew, 2017^[30]).

36. While off-label prescribing is unregulated in most, if not all, health systems, coverage by third-party payers may exclude use outside the approved indications for marketing. Medicines may also be prescribed for approved, but not (or not yet) covered, indications (referred to as *‘off-coverage’* or *‘off-formulary’* use). In some countries so-called early access or compassionate use schemes enable patients to access medicines for which formulary selection or coverage decisions have not yet been made. When a subsequent coverage decision is negative, patients may be expected to pay the full cost out-of-pocket at the point of care unless there are mechanisms available for providing exceptional access. Importantly, off-label and off-coverage use are very different; drugs approved for marketing but not (or not yet) covered have been determined to have a positive risk/benefit balance in the relevant (on-label) indication. Products used off-label may not be supported by substantive evidence of benefit, and may thus represent a greater risk to patients.

37. Table 2.3 presents the results of the OECD survey pertaining to the off-label use of medicines in health systems. While off-label use is not covered in a number of countries, it can be covered in some circumstances, most often where it addresses an unmet medical need, and with prior authorisation. In some countries, coverage of off-label use depends on the health care setting (e.g. Canada, Sweden).

Table 2.3. Coverage of off-label use of oncology medicines in OECD/EU countries

Off-label use possible, but not covered
Australia, Chile, Israel, Japan, Korea, Latvia, Lithuania, United Kingdom (England)
Sweden for outpatients.
Off-label use possible, and covered
Belgium, only for unmet need for new medicines. There are no coverage restrictions for older off-patent medicines used off-label.
Canada for inpatients. For outpatients, it depends on the health coverage scheme.
Cyprus: off-label use is possible and funded by the government
France: off-label used is covered by a temporary authorisation for use programme or under exceptional individual circumstances.
Estonia, via hospital service list, ambulatory list, or for individual patients under exceptional circumstances
Germany, if off-label indication approved by an expert group and health technology assessment body
Hungary and Greece with individual prior authorisation
Italy: off-label use is covered if there is unmet need, the company is not conducting clinical trials or there is no active compassionate use programme. Off-label access requires approval based on evidence of potential benefit and regulatory requirements.
Lithuania for ultra-rare diseases
Malta: cancer cases can be managed through exceptional treatment schemes, which are not specific to off-label use but may include it.
Norway, hospitals cover off-label use in their budgets
Sweden for inpatients
Switzerland for unmet need and with prior authorisation by insurers.
United States: off-label use can be funded by Medicare if the product is deemed reasonable and necessary for treatment.

Other

Denmark: Off-label use is possible for all public hospital medicines, but is not included in treatment guidelines (The Danish Medicine Council).

Ireland: off-label use can be incorporated into 'standard of care' treatment and related costs. For high-cost medicines, off-label use is only covered by private insurers

Norway: off-label use possible in private hospitals

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

2.3. Managing place in therapy and pricing combination regimens

38. Increasingly, approaches to treating many cancers involve the administration of a number of medicines with distinct but complementary mechanisms of action in combination or in close sequence, as part of a regimen that also seeks to minimise the emergence of drug resistance. The following sections discuss the issues around determining place in therapy, and of pricing products used in combination treatment regimens.

2.3.1. Most countries use HTA to determine place in therapy of new medicines

39. Countries were asked what policies or approaches, if any, they use to address the challenge of determining the place in therapy of new medicines¹⁷. The objective was to understand who makes decisions about place in therapy, and based on which criteria (see Figure 2.2). In most countries, decisions are based on some form of HTA. Thirteen countries reported that place in therapy was determined on the basis of clinical evidence, and nine that it was determined by cost-effectiveness. Eight countries said that place in therapy was determined by clinical guidelines, and not specified in coverage conditions.

40. Some countries appear in several categories. For example, in Australia, place in therapy is determined by the HTA process, based on clinical and cost-effectiveness evidence. Coverage conditions are determined via the HTA process. If cost were not a factor, or the decision were cost-neutral, the preferred option would be to have prescribers determine place in therapy based on clinical judgement. Canada and Belgium indicated that HTA entities provide recommendations on place in therapy to inform coverage conditions and potential restrictions. In Belgium this is more likely to apply to high-priced medicines.

41. In Norway, while the use of a drug may be described in clinical guidelines, the Decision Forum¹⁸ determines the conditions surrounding each new medicine's use. In some circumstances, the HTA process restricts coverage conditions to specific subgroups because of differences in cost-effectiveness. Place in therapy may be determined by cost-utility analysis. Where clinical trials show equi-effectiveness between medicines these may be subject to tendering. The oncology expert group then makes recommendations on place in therapy depending on the results of the tender.

42. In France, HAS determines the place of a drug in therapy as part of the HTA undertaken to inform the coverage decision and price negotiation. To do so, HAS uses clinical practice guidelines published in particular by the French National Cancer Institute (INCa).

¹⁷ Place in therapy refers to whether a medicine is to be used by itself or in combination, in what line of treatment, or in what sequence of treatment for a given stage of disease etc.

¹⁸ In Norway, coverage decisions for hospital drugs (all oncology treatments) are devolved to the four Regional Health Authorities, but they have in turn delegated this responsibility to a Decision Forum, whose decisions are de facto national ones.

43. In the United States, Medicare Part D plans are permitted to utilise both formularies and ‘step-therapy’¹⁹. The Centers for Medicare & Medicaid Services (CMS) issue guidance on how to determine the adequacy of a plan’s formulary, but the plans themselves set the step-therapy requirements. Medicare Advantage plans are also permitted to use step-therapy for their enrollees. Other private health insurance plans can freely determine coverage rules.

Figure 2.2. Approaches to determining place in therapy of new drugs across OECD/EU countries

Based on responses from 24 countries to the OECD survey (multiple options possible per country).

Note: HTA health technology assessment

In Chile, HTA determines place in therapy only for medicines covered through the High Treatment Cost Law, not for the private sector.

In Denmark, place in therapy is primarily determined by clinical guidelines, but can be determined by cost if two products have the same effectiveness.

Source: Authors based on 2019 OECD challenges in access to oncology survey.

2.3.2. Pricing of products used in combination treatment regimens remains a challenge

44. A related issue is the growing use of combination treatment regimens²⁰ in oncology. Increasingly, approaches to treating many cancers involve the concurrent administration of a number of products with distinct but complementary mechanisms of action in combination or in close sequence, as part of a regimen that also seeks to minimise the emergence of drug resistance. Combination approaches to oncology treatment have become the norm for both solid tumours and haematological malignancies, and are expected to proliferate over the next few years. Dankó et al. identified 16 products approved by the EMA for use in combination with other products by February 2019 (Dankó, Blay and Garrison, 2019^[31]). Some recent examples include the addition of pertuzumab to trastuzumab for the treatment of human epidermal growth factor receptor 2 (HER-2) positive breast cancer, and the use of programmed cell death protein (PD-1) and programmed cell death ligand (PD-L1) inhibitors in combination with anti-cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) therapies in metastatic melanoma. A recent study counted more than 1700 clinical trials for regimes involving anti-PD-1/PD-L1 with other cancer therapies (drug or non-drug) (Tang et al., 2018^[32]). For HTA bodies and payers, this trend presents serious challenges.

¹⁹ ‘Step-therapy’ is a type of prior authorisation in which a patient begins treatment for a specific medical condition by using the most preferred medication (usually the most cost-effective), and progressing to other therapies only if necessary (i.e. in the event of intolerance or treatment failure).

²⁰ Combination regimens refers to different medicines being used in combination, but not in a fixed dose product.

45. Standard approaches to HTA (determining whether an incremental cost-effectiveness ratio falls under an acceptable willingness to pay threshold) can produce results that are counterintuitive, or inconsistent with societal preferences. This was the case when the addition of a medicine to an existing treatment offering meaningful clinical benefit was nonetheless be found to be ‘not cost-effective at zero price’ (Davis, 2014^[33]). Pertuzumab for HER-2+ metastatic breast cancer offered an incremental overall survival benefit of 15.9 months when added to trastuzumab (Herceptin®), but NICE did not initially consider it to be cost-effective for use in the NHS even if the drug were provided free of charge.²¹ This was because the use of additional health resources (concomitant to improved survival) over and above the cost of the ‘backbone’ therapy, pushed the total treatment costs beyond what was considered acceptably cost-effective at the margin.

46. From payers’ and decision makers’ points of view, the most common situation can be described as follows (illustrated in Figure 2.3): products A and B are already in the market and have different modes of actions or targets. The sponsor of product B obtains marketing authorisation for the use of its product in association with product A and files an application for coverage of the combination. Product A is usually referred to as the “backbone” therapy (irrespective of its contribution to the clinical benefit of the combination) and product B as the “add-on therapy”, while both products are “the constituents” of the combination (Dankó, Blay and Garrison, 2019^[31]).

Figure 2.3. Setting prices of products used in combination regimens

Source: Authors.

47. Often the sum of the respective prices of drugs A and B exceeds the willingness to pay for the combination regimen. Decision makers may then decide not to cover the combination, or they may choose to restrict access to it, but if there is an incremental benefit for patients, a solution is likely to be pursued. If the two products are made by the same manufacturer, a pricing agreement may be easier to reach, even though—as with indication-based pricing—it may be challenging to operationalise. However, the issue is more complex when the constituent products are marketed by different companies. The first issue is

²¹ NICE was ultimately able to issue a positive recommendation in the final guidance, and the initial assessment is intended to be illustrative.

determining the value of each product when used in combination;²² the second is compliance with competition law.

48. In general, the company selling the backbone product has an interest in the combination being covered because it is expected to retain or even increase sales of its product. The company may therefore be willing to reduce the price of A in that indication if it does not affect the price of A in other indications. If the price of A is potentially affected in all circumstances (because the payer is unable or unwilling to use indication-based pricing), the company may be reluctant to accept a lower price if it is not fully compensated by the anticipated increase in uptake arising from the use of the combination of A+B.

49. A key issue is how the prices of A and B in the combination regimen should be determined. The approaches reported by countries are described in Table 2.4. It appears that combination regimens are generally assessed using standard methods of evaluation, and with the possible exception of Australia, HTA entities do not, as a rule, attempt to attribute value shares to the constituent products. In some countries, for example Belgium, the company filing the application for coverage or pricing is expected to adjust its price to make the price of the combination acceptable to payers.

50. From a legal perspective, competition law generally prohibits companies from mutually agreeing on prices for their products, particularly if they are in competition, unless there are demonstrable benefits to consumers from doing so. Companies agreeing on prices of products used in combination regimens are breaking the law if (i) the products are competitors, rather than complements; or (ii) if they are complements but the combination is used to foreclose access to one of the products or competitors of the suppliers. Within these constraints, pharmaceutical industry associations (both regional and national) within Europe have been working to identify practical solutions for adapting the prices of constituents of combination regimens.²³ So far, countries have adopted a variety of approaches. In France, the pricing committee determines its willingness to pay for the combination and then negotiates individually with each of the companies. In Switzerland, the price of the combination is determined and public authorities then negotiate (confidential) prices with individual companies.

51. In the United Kingdom (England), the Department of Health and Social Care (DHSC) and NHS England are waiting for proposals from Association of the British Pharmaceutical Industry (ABPI) “to allow company-to-company engagement, to ensure that the combined cost of combinations can be developed for NICE appraisal, at the standard NICE threshold, in line with competition law” (Department of Health and Social Care and ABPI, 2018, p. 27^[21]).

²² Value is used here as a generic term. It may refer to clinical benefit, to cost-effectiveness, or to any metric chosen to represent value in a specific environment.

²³ See for instance (Sandmeier, 2017^[98]) (EFPIA, 2018^[99]).

Table 2.4. Approaches to attributing value to constituents of combination regimens in OECD/EU countries

Country	Approaches to attribute value to constituents
Australia	This is highly context specific. First, the cost-effectiveness of the combination is determined based on the price proposed. Attributing value to the constituent parts will be influenced by relevant factors, including: <ul style="list-style-type: none"> - whether used concomitantly at all times, whether used in an overlapping way (e.g. use of one medicine extended as “maintenance”), or whether used entirely in sequence - whether one medicine is already listed for the target population and thus has an already established price, and if so, whether this price is likely to change in the near future - whether the constituent medicines are supplied by the same company, or by competing companies. Relevant factors such as these influence first the PBAC deliberations in deciding whether to recommend listing, and subsequently the government negotiations and decisions about whether to implement the PBAC’s recommendation to list.
Belgium	No specific approach. In general if a company applies for coverage of its product B to be used with A, it will be expected to cover the cost of A, and the price of A is unlikely to change.
Canada	The HTA body assesses the combination therapy to issue a recommendation for public plans. The review looks at the product as a combination and does not focus on the constituent parts individually, to develop a funding recommendation. Typically, economic analyses by CADTH ensure that public plans are not paying more than the aggregate of the current costs of the individual components.
Chile	No approach to attribute value to individual constituents of the combination. Budget impact is taken into account in price negotiations, which typically consider volumes rather than value.
France	The HTA body assesses the application for coverage of B, used in association with A and determines the added therapeutic benefit of A+B over the comparator (which might be A alone). The pricing committee then negotiates the price of the combination <ul style="list-style-type: none"> - If the combination has a minor added benefit (level IV), the cost of (A+B) must be = previous cost of A. - If the combination has a greater added benefit (from moderate III to major I), the cost of (A+B) may be = to the cost of A + 10% or more. In all cases, both prices must be negotiated. Treatment costs are based on net cost if any rebate. The price negotiation is done for each indication. Authorities do not attribute a share of the ‘value’ to constituents; the pricing committee negotiates with individual companies separately and may use confidential discounts.
Germany	The comparator therapy is the basis to determine the benefit for a new medicinal product and negotiate price if needed.
Hungary	Based on cost-effectiveness analysis and budget impact analysis and recommendations of Therapeutic Committee (financing protocols).
Italy	AIFA negotiates the price of a new product, regardless of its use in combination with other medicines. However, different types of MEAs can be applied to the product used in combination with other medicines, through the implementation of a patient monitoring registry. In such cases, the net price (i.e. list prices minus any agreed discounts) of the combination regimen may be different from the price of the single components used in other indications. When one of the medicines in the combination regimen is already reimbursed by the national health service, its price is generally considered a fixed parameter (although price negotiations can occur) and the price of the second part of the combination is defined so that the total cost of the combination reflects its added value. This approach is not mandatory for pricing decisions made by the Pricing & Reimbursement Committee.
Latvia	If both products are from the same company, the price is set for the combination and coverage restrictions may be applied stating that the products are reimbursed only if used in combination. If the new product is added to an existing therapy (which is the comparator) the price of a new product is approved based on cost-effectiveness assessment.
Lithuania	The combination is assessed as it would be for a monotherapy
Norway	No specific approaches used to valuing constituent parts of combination treatment regimens.
Sweden	The Dental & Pharmaceutical Benefits Agency (TLV) is currently working on the development of a method to price combinations therapies, with consultation in relevant stakeholders, including regions and industry.
Switzerland	Comparison of the combination therapy with the existing Standard of Care. For clinically relevant additional benefits, an innovation premium can be considered (max. 20 % over the price of the comparator). The cost-effective price per month of progression-free survival is used to calculate the price of the combination and then the payback for single agents.
United Kingdom (England)	NICE does not undertake value attribution between constituents of combination therapies; this needs to be established prior to appraisal submission to NICE. Along with DHSC, NHS England and NHS Improvement, NICE expects to support ABPI’s efforts to enable companies to engage with one another where health-improving combination therapies face challenges coming to market, and ensure that the aggregate cost of combinations can be developed for NICE appraisal, within the standard NICE threshold, and in line with competition law.

Note: PBAC Pharmaceutical Benefits Advisory Committee, HTA health technology assessment, CADTH Canadian Agency for Drugs and Technologies in Health, AIFA Italian Medicines Agency, DHSC Department of Health & Social Care, MEA managed entry agreement, TLV The Dental and Pharmaceutical Benefits Agency, NICE National Institute for Health and Care Excellence, NHS National Health Service, ABPI Association of the British Pharmaceutical Industry.

Ireland and Malta, responded that no specific approach has been defined yet.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

2.4. Managing increasing treatment costs within budget constraints

52. While fast-paced innovation in oncology is good news for patients and societies, many health policy makers are concerned about its impact on health expenditures and on the equitable allocation of resources within the health sector. The following sections examine general trends in pharmaceutical expenditure, and explore special financing arrangements for oncology medicines used in a few countries.

2.4.1. Many new medicines are coming to market, with increasing launch prices

53. The number of new oncology medicines and indications has been increasing rapidly, especially since 2010. The EMA has approved 10 cancer medicines each year over the past decade (see Figure 2.4 panel A and (Hofmarcher et al., 2019^[4])). In parallel, the launch prices of oncology medicines have also rapidly increased. In the United States, the average monthly cost of treatment has constantly increased over time and some new treatments cost nearly USD 85 000 per month (see Figure 2.4 panel B and (Bach, 2019^[34])). Moreover, the figures do not take into account two of the new CAR-T treatments, Kymriah® and Yescarta®, both approved in 2017, and costing USD 216 564 and 170 060, respectively for one-off treatment. In Canada, the share of medicines with monthly treatment costs exceeding CAD 10 000 now accounts for almost one third of oncology sales (see Figure 2.4 panel C and (NPDUIS, 2019^[35])).

54. The prices of new oncology medicines have been questioned by many stakeholders, including prescribers, third-party payers, and civil society, and concerns have been echoed in conference proceedings, media coverage²⁴ and investigations by various institutions.²⁵ In April 2019, the UK Institute for Cancer Research (ICR) published a very strong position statement, noting that there are “fundamental problems with the way that cancer drugs are priced, [and that as a result] many innovative new medicines end up being unaffordable for health care systems”, and calling for “a new approach to pricing that sets a fair price for each drug – taking into account the need for a return on investment, but without pushing health care systems to the limits of what they can afford.” (ICR, 2019, p. 1^[36]).

²⁴ See for example: <http://sante.lefigaro.fr/actualite/2016/03/14/24739-lurgence-maitriser-prix-nouveaux-medicaments-contre-cancer>; <https://www.theguardian.com/science/2017/dec/20/drug-giants-hefty-prices-nhs-vital-medication-pharma-profits>; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6745980/pdf/hs9-1-e12.pdf>; <https://www.irishexaminer.com/breakingnews/ireland/cancer-patients-under-siege-from-treatment-costs-936549.html>; consulted on 18 March 2020.

²⁵ See <https://www.lecese.fr/travaux-publies/prix-et-acces-aux-medicaments-innovants>, consulted on 18 March 2020.

Figure 2.4. Trends in the number of oncology medicines approved and their prices**A: Number of cancer medicines and indications approved by the European Medicines Agency, 1995-2018**

Source: Reproduced from (Hofmarcher et al., 2019^[41]), Comparator Report on Cancer in Europe 2019, <https://ihe.se/en/publicering/comparator-report-on-cancer-in-europe-2019/>, on 26 February 2020.

B. Monthly costs of cancer drugs at time of US FDA approval, 2000-2019

Note: Based on Medicare reimbursement rates and by year of drug approval. Median cost is computed for 5-year period. Figure excludes Kymriah® and Yescarta®, both approved in 2017.

Source: Reproduced from (Bach, 2019^[34]), Prices & Value of Cancer Drugs, <https://www.mskcc.org/research-programs/health-policy-outcomes/cost-drugs>, on 17 March 2020.

C: Sales revenue share by 28-day treatment cost (CAD) of oncology medicines, Canada, 2009 to 2018

Source: Reproduced from the Patented Medicine Prices Review Board (PMPRB) (NPDUIS, 2019^[35]), The oncology drug market: A high-growth, high-price therapeutic area, <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1453&lang=en>, on 27 February 2020. The reproduction is a copy of an official work that is published by the Government of Canada and that the reproduction has not been produced in affiliation with, or with the endorsement of the Government of Canada.

2.4.2. Increases in expenditures have been partly compensated by savings in other parts of the health system

55. Expenditures on oncology medicines are not only impacted by increasing prices but also by increasing numbers of patients being treated, the result of the increasing prevalence of some cancers and evolution in treatment options (Hofmarcher et al., 2019^[4]). As a result of these trends in volumes and prices, the value of sales of oncology medicines more than doubled in Europe in the past decade²⁶, and in the United States in just five years²⁷ (Hofmarcher et al., 2019^[4]; IQVIA, 2019^[37]). Available sales data, however, are not an ideal source for estimating pharmaceutical expenditures. To begin with, they do not include distribution mark-ups and taxes on medicines sold to outpatients for self-administration (thereby underestimating the impact on health care budgets). Nor do they take into account confidential ex-post rebates, which are particularly important in oncology markets (thereby overestimating the impact on health expenditures). As a matter of fact, only a handful of countries are able to report trends in expenditure on oncology medicines. In Italy, where data on public expenditure and sales can be compared, the differences are not negligible (public expenditure was 26% lower than sales in 2018) (see Figure 2.5). However, the difference is unlikely to be due to private expenditure alone, but can be attributed in part to product-specific rebates (Osmed/AIFA, 2019^[38]).

²⁶ Sales growth at list prices, in real term between 2008 and 2018, according to (Hofmarcher et al., 2019^[4]). These series do not take into account ex-post rebates.

²⁷ Sales growth at list prices, current prices according to (IQVIA, 2019^[37]).

Figure 2.5. Comparisons of expenditures and sales per capita for oncology medicines in Italy

Source: Authors based on per capita public expenditure on oncology medicines, in current euros, taken from (Osmed/AIFA, 2019^[38]); and per capita sales in current euros taken from (Hofmarcher et al., 2019^[4]).

56. Without appropriate monitoring of expenditure on oncology medicines, the impact of consumption and price trends on total pharmaceutical or total health expenditures is not easy to discern, and requires a lot of estimation and assumptions (Hofmarcher et al., 2019^[4]). What can be observed is that expenditure on *retail* pharmaceuticals as a share of Gross Domestic Product (GDP) has remained stable over the past decade in OECD countries. This is due in part to a combination of market dynamics (generic and biosimilar competition) and cost-containment policies. However, this does not provide a complete picture of current trends. In several countries, expenditure on medicines administered as part of an outpatient or inpatient service accounts for a substantial share of total pharmaceutical expenditures (e.g. 26% in Greece, 30% in Israel, 39% in Portugal, and 44% in Denmark). Moreover, this spending is increasing much more rapidly than that of retail pharmaceuticals (see Figure 2.6).

Figure 2.6. Trends in pharmaceutical expenditure**A: Retail pharmaceutical expenditure, as share of GDP, 2007-2017** **B: Total pharmaceutical expenditure, as share of GDP, in 2017** **C: Growth of expenditure of retail and hospital pharmaceuticals 2007-2017**

Note: Panel A: Retail pharmaceutical expenditure includes medical non-durables. * latest year available 2016; ** 2014; *** first year available 2010. Panel C: Average annual growth of expenditures, in real terms

Source: OECD Health Statistics 2019

2.4.3. Some countries have special financing arrangements for oncology medicines

57. In response to the OECD survey, several countries reported having special financing mechanisms for high-cost drugs, but only six countries²⁸ reported having established arrangements specifically for the financing, pricing and procurement of oncology medicines:

- In Canada, provincial and territorial governments are responsible for the delivery of health services, including determining the covered medicines and applicable conditions. Some sub-national governments have established cancer agencies with earmarked budgets to deliver treatment. These budgets typically cover all cancer care, including medicines.
- Italy and England have both adopted approaches involving earmarked funding for new oncology medicines, prior to their inclusion in routine health care budgets.
 - In Italy, an annual fund of EUR 500 million, renewable every three years, has been made available since 2017 for “new, innovative” oncology medicines. Eligible medicines must be determined to be “innovative” according to well-defined criteria that include offering added therapeutic value compared to existing treatments (see Box 2.3). First-in class medicines may benefit from this status for a maximum of 36 months. Follow-on products may be eligible but only for the residual period up to 36 months. The system is demand-driven. If the financing of eligible treatments exceeds EUR 500 million in a given year, companies must pay rebates. In 2018, expenditure on these medicines (net of MEA rebates, but before fund-specific rebates) amounted to EUR 613.8 million (Osmed/AIFA, 2019^[38]). Importantly, medicines funded via this mechanism are excluded from the estimation of pharmaceutical expenditure that is subject to the total pharmaceutical expenditure cap (OECD, 2019^[39]). The renewal of this earmarked fund is currently being discussed.
 - In England, the ‘new’ Cancer Drugs Fund (CDF) covers new oncology medicines under three scenarios (see Figure 2.7): medicines with a marketing authorisation awaiting NICE appraisal (through Interim Funding Arrangements); medicines supplied via Managed Access Agreements through the CDF while further data are collected to reduce uncertainty (usually for a period of two years); and medicines approved by NICE for routine NHS commissioning, for a period of 90 days following the decision. The annual budget for the CDF is GBP 340 million, beyond which all companies with medicines funded through it must pay rebates in proportion to their own sales (NHS England Cancer Drugs Fund Team, 2016^[40]; NICE, 2018^[41]; NICE, n.d.^[42]).
- In Chile, the 2016 “Ricarte Soto law” established a fund for high cost treatments and diagnostics, and a specific fund for cancer drugs is currently under discussion in the Chilean Parliament. The system enables the financing of one type of medicine or device per disease and invites companies to submit confidential proposals to the Ministry of Health (MOH). Once a medicine is selected, the MOH sends the information (prices and conditions) to the National Procurement Agency (CENABAST) who opens a public bidding process, or purchases directly when there is only one possible provider. All companies can participate, but their bid may not be less favourable than that previously presented to the MOH.²⁹

²⁸ Greece and Malta reported earmarked funding for oncology medicines. In Malta, a specific oncology financial vote was introduced in 2017 for new oncology medicines to be introduced on the Government Formulary, as approved and prioritised by the Ministry for Health

²⁹ <https://www.minsal.cl/ley-nacional-de-cancer-fue-aprobada-en-general-por-el-senado/>

Box 2.3. Criteria used to determine eligibility for funding through Italy's Fund for Innovative Medicines in Oncology

"Innovative" oncology medicines are currently financed through a specific fund "*Fondo per i farmaci innovativi oncologici*" (Law n. 232/2016, art.1), which, since 2017 provides EUR 500 million per year for three years and is renewable every three years. The Italian Medicines Agency (AIFA) has defined criteria for identifying "innovative" medicines (Det. 1535/2017) taking into account: (1) therapeutic need; (2) added therapeutic value; and (3) the quality of evidence and robustness of clinical studies.

(1) Therapeutic need is scored on a 5-level scale from "maximum" (absence of any therapeutic option) to "absent" (presence of therapeutic alternatives for the specific indication able to modify the natural history of the disease and with a favourable safety profile).

(2) Added therapeutic value is defined as the extent of the clinical benefit offered by the new medicine compared to existing alternatives, assessed against outcomes that are clinically relevant and validated for the condition treated. The added therapeutic value is also scored on a 5-point scale from "maximum" (greater efficacy demonstrated on clinically relevant outcomes; the medicine is able to cure the disease or change its natural history) to "absent" (absence of an additional clinical benefit compared to therapeutic alternatives available).

(3) Quality of evidence and robustness of clinical studies. For the evaluation of this parameter, AIFA uses the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system to assess the quality as High, Moderate, Low, or Very low.

Source: <http://www.agenziafarmaco.gov.it/content/criteri-la-classificazione-dei-farmaci-innovativi-e-dei-farmaci-oncologici-innovativi-180920> ; <http://www.jclinepi.com/content/jce-GRADE-Series>

Figure 2.7. The role of the Cancer Drugs Fund in the English National Health System

Note: HTA health technology assessment, CDF Cancer Drugs Fund (England), NICE National Institute for Health and Care Excellence, NHS National Health Service (England)

Source: Authors, based on information provided by NHS England and NICE (NHS England Cancer Drugs Fund Team, 2016^[40]; NICE, 2018^[41]; NICE, n.d.^[42]).

58. These earmarked funds seem to function as a “double guarantee”: a guarantee that selected new treatments will be available in the system, and at the same time, a guarantee that they will not capture a disproportionate amount of resources. However, concerns have been raised by other countries on the equity of such earmarked funds.

59. Other countries mentioned special financing arrangements which are not specific to oncology medicines but aim to fund *early* or *exceptional* access to some medicines. In Belgium, for example, Early Temporary Authorisation for use and Early Temporary Reimbursement schemes can be used to provide subsidised access to promising therapies used in severe/fatal diseases with no covered alternative treatments. The indication must be included in the “Unmet Medical Need list”, updated annually. The system is demand driven. In addition, a Special Solidarity Fund provides a further safety net to cover high cost treatment for rare diseases excluded from the universal insurance system. Several criteria have to be met to be eligible for coverage and the budget of this fund is limited. France also has special arrangements which aim to fund early or exceptional access to some medicines: ATU (authorization for temporary use) and RTU (recommendation for temporary use).

60. Finally, two countries responded that **procurement processes** for oncology medicines differed from that of other medicines. In Canada (except in Quebec), hospitals undertake their own procurement processes and often have dedicated budgets for cancer care. In Latvia, centralised procurement is organised by the National Health Service for chemotherapy medicines.

2.4.4. Promoting competition in off-patent markets can save costs and increase access

61. Once market exclusivity is exhausted, competition from generics or biosimilars is expected to result in lower prices and cost savings. Usually, the price difference between originator and generic is higher than that between originator and biosimilar (up to 80% versus 15-30%, respectively) (Simoens, 2011^[43]; Nabhan et al., 2018^[44]). However, potential savings are high given that biologic prices are generally higher than small molecules and that the market share of biologics is increasing.

62. Recent studies have looked at generic prices and savings after generic entry for simple molecules or groups of molecules. Lejniece et al. reported that in Latvia, the annual cost of generic imatinib was 96% lower than that of the originator (Lejniece, Udre and Rivkina, 2017^[45]). In the United Kingdom, the uptake of generic versions of imatinib saved the NHS GBP 66.3 million in the year 2017-2018 (NHS England, 2018^[46]). Godman and Simoens (2019^[47]) looked at nine generic oral cancer medicines included in the World Health Organization’s (WHO) *Model List of Essential Medicines* across 25 EU countries. They observed that as a result of generics policies, differences between originator and generics prices varied widely between countries. For example, for capecitabine in Norway, France, Spain and Sweden the differences were 45%, 53%, 67% and 80%, respectively (Godman and Simoens, 2019^[47]). In Japan, where generic market penetration was relatively high for oncology medicines between 2010 and 2016, it was relatively low for antimetabolites, protein kinase inhibitors, hormones, and with no penetration of monoclonal antibodies (likely not yet off-patent) (Shibata et al., 2017^[48]).

63. In Europe, at least one biosimilar is available for each of three biologics used in oncology and four used in supportive care (European Medicines Agency, 2019^[49]). Hofmarcher et al. (2019^[4]) estimated the potential cost savings from biosimilars from the three biologics (bevacizumab, rituximab and trastuzumab) at EUR 2.4 billion in Europe per year, based on sales in 2016 (before the first biosimilar was approved) and assuming a 45% price reduction compared to the reference product. In 2018 in Europe, these three medicines accounted for 15% of all cancer medicine sales.

64. A range of contextual factors may influence the magnitude of price reductions following the introduction of generic / biosimilar medicines, and the extent of generic / biosimilar uptake (World Health Organization, 2018, pp. 64-67^[2]; Godman and Simoens, 2019^[47])

65. In 2014, Kanavos outlined a methodological framework for measuring performance in off-patent drug markets in 12 EU Member States. Performance indicators include generic availability (12 and 24 months after patent expiry), time to generic entry, number of generic competitors, generic price development and impact, and generic volume market share. According to these indicators, the Netherlands, Denmark, Germany and the United Kingdom have high-performing generic markets (Kanavos, 2014^[50]).

66. For each of the 109 product/indication pairs in the sample in Part 3 of the OECD survey, respondents were asked if the originator / reference product was currently protected from generic or biosimilar competition, and if not, the number of generic/biosimilar products available for that indication (see Annex A. for further details). Responses to this part of the survey were incomplete; of those product/indication pairs approved in each country, the numbers reported as no longer protected ranged from 34 (in Hungary) to 55 (in Sweden), with at least one generic / biosimilar available in most countries (see Figure 2.8). The United Kingdom (England), Germany and the United States had the highest proportions of product/indications with more than five generics / biosimilars available, with 92%, 61% and 58% respectively. This confirms what is already known about the strength of generics markets in these countries. Of note was the considerable proportion of product/indications reported as “no longer protected”, but for which no competitor had entered the market, i.e. 28% in Denmark, and 35% in Japan.

67. The number of product/indication pairs no longer protected may vary across countries for a number of reasons. Firstly, the duration of protection from competition depends on national or regional legislation (differences in patent expiration dates, and the commencement and duration of regulatory exclusivity periods). In most countries, data or market exclusivity terms begin on the date of marketing approval in the country or region (Copenhagen Economics, 2018^[51]). Once product/indications are no longer protected, time to generic entry will depend in part on local policy settings. Some countries (eg. Germany) have no formal pricing and coverage procedures for generics and biosimilars, and can therefore benefit from competition very soon after generic marketing approval.

Figure 2.8. Percentage of products reported as no longer protected from competition, by number of generics/biosimilars available across OECD/EU countries

Note: Data from Chile, Estonia, Lithuania, Malta, and Norway were excluded as data were not representative.

Source: Authors based on 2019 OECD challenges in access to oncology survey.

2.4.5. Reducing waste and optimising dosage can also generate savings

68. Savings can also be achieved by minimizing wastage of high-cost (injectable) cancer medicines. Dosages are often individualised, based on patient body weight or surface area. Each dose must be made up specifically for the patient, using a combination of vial sizes (where available). As a result, there may be leftover drug that is subsequently wasted as it must be discarded within a short time (based on the stability data of the drug, and often within a few hours). Bach et al (2016^[52]) examined the top 20 cancer drugs that are dosed by body size and packaged in single-use vials, and estimated the extent of leftover product, based on 2016 US sales. The proportion of leftover drug varied from 1% to 33% across the products, representing 10% of companies' revenues from these medicines, or USD 1.8 billion. The cost for consumers and third-party payers was higher since it included supply chain mark-ups (Bach et al., 2016^[52]). Pearson, Ringland, & Ward (2007^[53]) examined wastage of trastuzumab, used for the treatment of metastatic breast cancer, in Australia. Trastuzumab is dosed by patient body size and was only available in one vial size at that time. An estimated 24% of trastuzumab dispensed over a 40-month period from December 2001 to March 2005 was discarded. This amounted to AUD 21.1 million. Alternative dosing schedules and the availability of another vial size were estimated to reduce wastage to 5% of volume dispensed (Pearson, Ringland and Ward, 2007^[53]). Subsequently a smaller vial size was registered.

69. Two studies highlighted a number of strategies for reducing wastage, generally aimed at pharmaceutical companies (Gilbar and Chambers, 2017^[54]; Gilbar et al., 2019^[55]). They included: 1) increasing the range of vial sizes available in countries; 2) ensuring vials contain excess or overage of the drug to compensate for loss during manufacture resulting in insufficient volume of the drug for a patient dose; 3) further research to provide extended stability data, as most oncology medicines have short expiry dates once reconstituted due to lack of information on stability; and 4) ensuring medicines are available in the most appropriate form (e.g. pre-filled syringes or pens) (Gilbar and Chambers, 2017^[54]; Gilbar et al., 2019^[55]). An additional method aimed at pharmaceutical companies would be to encourage the manufacture of vial sizes that reflect fixed dosage regimens. Other proposed methods include vial sharing, whereby leftover drug from one patient can be used in the preparation of a dose for another patient. While vial sharing reportedly occurs in Australia, it is not a specific Australian strategy to reduce wastage. In addition, optimising treatment doses may be another step in reducing the financial toxicity of cancer medicines. This includes optimization of dose, duration, and type of drug (The Lancet Oncology, 2018^[56]; Norris, 2018^[57]).

70. Since 2011 in Australia, the Efficient Funding of Chemotherapy Program aims to minimise wastage and reduce payer and patient costs of injectable cancer medicines administered in public and private hospitals. Prescribers order per treatment doses for each patient (e.g. in milligrams), rather than by vial; the programme provides national Pharmaceutical Benefit Scheme (PBS) reimbursement to pharmacies based on supplying the lowest cost combination of vials for this dose (Australian Government Department of Health, 2019^[58]; 2013^[59]). Even though a 2013 review of the programme found that the funding arrangements did not align with the complexity of chemotherapy pharmaceutical provision models in Australia and highlighted the complexity and administrative burden of PBS reimbursement, the programme remains in place (Australian Government Department of Health, 2013^[59]).

3. Assessing access to oncology medicines in OECD/EU countries

71. Variation in access to oncology medicines across countries may reflect differences in the capacities of, and resources available in health care systems (administrative, technical, and financial), in willingness to pay for oncology medicines, and in societal priorities regarding cancer care *vis a vis* other diseases. Additionally, countries may vary in terms of the level and nature of the payer making the coverage decision, the extent of coverage provided, and the amount that patients are expected to contribute to the costs of their care. The following section discusses the dimensions of access, and presents the results of the OECD's survey on regulatory approval, coverage status and time to access³⁰ for a selected sample of oncology medicines. Potential reasons for differences in access are explored, as are sources of inequity and patient expectations.

3.1. Access is multi-dimensional

72. Access to oncology medicines can be assessed across three major dimensions: availability, affordability, and accessibility, defined below. Broad access to *all* cancer medicines is often assumed to be ideal, but is not essential. Access must be considered within the context and characteristics of each country's health care system. For example, if several medicines are potentially available for a given indication, procurement policies and methods might result in only some of them being available, without necessarily disadvantaging patients. Moreover, even in countries without significant or absolute budget constraints, it may be challenging (or even illegal) for coverage to be provided for medicines not demonstrated to be cost-effective.

3.1.1. Availability in the market is the first step

73. Availability in the market is the first essential condition for ensuring access to medicines. This is generally predicated on the granting of *marketing authorisation* for a product (for one or more specific indications), followed by *launch of the medicine* by the manufacturer. While companies often launch products as soon as marketing authorisation is granted, in some countries they may choose to wait for a decision on funding by one or more third-party payers (government or health insurance), and this will often be linked to some form of price regulation. In terms of availability and timeliness of the availability of a medicine in a given country, the following indicators are pertinent:

- Whether the medicine has marketing authorisation (i.e. regulatory approval);
- Whether the product has been launched on the market by the manufacturer;
- The elapsed time between marketing authorisation and launch; and
- The elapsed time between first approval/launch and approval/launch in a given country. This is in turn influenced by two factors: the launch strategy of the company (influenced by market size and

³⁰ In this study, "time to access" for a medicine (or an indication) was generally measured as the time between submission of the application for marketing authorisation in the country (or region for EU) and the date of the coverage decision.

pharmaceutical policies in each country, as shown in Danzon and Epstein (2012^[60]), and the nature and performance of the regulatory and coverage decision-making processes.

3.1.2. Affordability at the individual and societal level must follow

74. Affordability can be considered at the individual level, for patients or their families, and at the societal level (for public budgets). For the overwhelming majority of oncology medicines, funding by third-party payers is essential for individual affordability. In most OECD countries, these medicines are covered by government or health insurance schemes, albeit often with user charges or co-payments. To maintain affordability for patients, it is essential that 1) the medicine is covered, and that 2) user co-payments, where they exist, are not excessive. Affordability for health care systems may be influenced by government priority setting and resource allocation, which in turn are influenced by societal values and the priority afforded to health care relative to other social policy areas such as education and social welfare.

75. Indicators of affordability include the coverage status of the medicine and the insurance status of the patient, as well as the type and level of cost-sharing for different goods and services (e.g. co-payments, co-insurance, deductibles, extra-billing, safety nets or caps), other out-of-pocket costs to patients, and individual drug prices. These are defined and discussed in section 3.6.

3.1.3. Accessibility ensures that eligible patients are actually treated

76. Accessibility encompasses the ability to obtain and fill a prescription for the medicine, as well as factors that influence the pathway to the patient—such as the inclusion in clinical guidelines and/or treatment protocols. Issues with the pharmaceutical supply chain, such as medicine shortages, also affect accessibility. The extent of use of a medicine by the patients for whom it is potentially of benefit would arguably be an ideal metric of accessibility, but unfortunately, this is not readily measurable. Other indicators might include:

- Utilisation in the general population, measured in standard units such as defined daily dose (DDD³¹) per 1000 population per day. This, however, does not take prevalence of disease into account.
- Proportion of eligible patients treated with the medicine. This indicator is a closer proxy for accessibility, but the number of eligible patients may be difficult to ascertain. Information on prevalence is most often insufficiently granular (by cancer type, stage, line of treatment) to compute the exact number of patients eligible for a given treatment.
- “Sales per dying patient”, has been used in the Comparator Report on Cancer in Europe (2019^[4]). It is the ratio of quantity sold (in milligrams) to the number of deaths from the cancers for which the medicine has an indication, as a proxy for incidence. Mortality data, however, may not reflect the number of patients treated.

³¹ The defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults.

3.2. Measuring access to oncology medicines is methodologically challenging

77. Experts from 23 OECD countries and EU Member States³² responded to the section of the OECD survey that sought information on aspects of access such as regulatory approval (i.e. marketing authorisation) and coverage, for a sample of 109 oncology product/indication pairs across five cancer types (including supportive care).

3.2.1. The OECD sample survey covered 109 product/indications pairs in 5 cancer types

78. The list of products and indications in the survey drew on the results of two European Society for Medical Oncology (ESMO) surveys that, to date, have produced the most comprehensive dataset on availability and coverage of cancer medicines across countries (Cherny et al., 2016^[61]; Cherny et al., 2017^[62]). In developing the OECD survey, the sample of medicines was narrowed to treatments for cancers with significant prevalence in OECD countries and EU Member States, albeit with the addition of one haematological malignancy. In order to capture the availability of novel medicines, any additional medicines for the selected indications approved in the United States or Europe as of July 2019 were added to the sample, as well as all oncology medicines included in the World Health Organization's 21st *Model List of Essential Medicines* (WHO-EML) (2019^[63]). The final list of indications comprised metastatic breast cancer, non-small cell lung cancer, colorectal cancer, melanoma, and multiple myeloma. Further details about the survey are presented in Annex A, with the final sample of products and indications shown in Table A A.2. Product/indications included in the WHO-EML, as well as those products approved in the United States since 2014 are flagged.

79. Product/indication pairs were further classified in order to facilitate the interpretation of availability of medicines and make a qualitative assessment of access. A qualitative judgement requires a framework for the classification of medicines into relevant categories. Hofmarcher et al. (2019^[4]) proposed several options, such as the class of the medicine (Anatomical Therapeutic Chemical [ATC] subgroups); the type of therapy (chemotherapy, targeted therapy, immunotherapy); the indication (lung cancer, colorectal cancer); the extent of unmet need or target population size (orphan drugs); the “vintage” (older vs newer medicines); and the therapeutic value (e.g. using classification systems proposed by ESMO, the American Society of Clinical Oncology [ASCO], and others).

80. For this analysis, two options were considered, in addition to inclusion in the WHO-EML, to provide a qualitative assessment of access:

- The ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS): This scale measures the therapeutic value of medicines (see Box 3.1 for more detail) (Cherny et al., 2015^[64]). It was created to highlight the most important drugs in terms of clinical benefit, in order to assist countries in prioritising access to these medicines. The Essential Medicine List Cancer Medicines Working Group, an informal advisory group who convened on 22-23 March 2018 to assist in the preparation of the WHO report *Pricing of Cancer Medicines and its Impacts*, proposed the use of this scale in considering therapies for listing on the WHO-EML (World Health Organization, 2018^[2]). However, the ESMO-MCBS could not be used for the OECD sample, because it does not provide scores for all products contained in the sample and because the ESMO scores individual indications in a very granular way (e.g. different line of therapy, different comparators). It was not possible to aggregate the scores to reflect the indications specified in the sample.

³² Responses were received from Australia, Belgium, Chile, Cyprus, the Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Israel, Japan, Korea, Latvia, Lithuania, Malta, Norway, Sweden, Switzerland, the United Kingdom (England only), and the United States.

- The ATC classification system developed by the WHO Collaborating Centre for Drug Statistics Methodology (WHOC) (WHO Collaborating Centre for Drug Statistics Methodology, 2019^[65]): Medicines were grouped by therapeutic class (ATC 4 level) in tables presenting information on availability and accessibility. At this level medicines have similar modes of actions and can often be considered as therapeutic alternatives.

Box 3.1. ESMO – Magnitude of Clinical Benefit Scale (ESMO-MCBS)

The European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) is a standardised, generic, validated tool to classify new cancer medicines according to their therapeutic value (Cherny et al., 2015^[64]; Cherny et al., 2017^[66]). The scale grades cancer medicines in curative and non-curative settings, based on their quality, efficacy and safety; it does not take cost into account. It was created in order to highlight the most important drugs in terms of clinical benefit, and increase access to such drugs. The table below outlines the grading system. A different form is completed based on the intent of the treatment (curative and non-curative) and the primary endpoints used to assess clinical benefit (e.g. overall survival, progression free survival, response rate etc.) Scores A and B in the curative setting, and 5 and 4 in the non-curative setting indicate grades with substantial improvement.

Table 3.1. ESMO-MCBS Treatment Scores

	Curative intent	Non-curative intent	
Scores	A	5	} High level of clinical benefit
	B	4	
	C	3	
		2	
		1	

Source: Adapted from (Cherny et al., 2015^[64]; Cherny et al., 2017^[66]).

ESMO-MCBS can be used by health technology assessment bodies for coverage decision-making, by prescribers and patients in daily practice, and in the design of clinical trials. Australia, for example, references this scale when prioritising oncology medicines for national medicine listings. Users can filter results of grading system by therapeutic agent, tumour type/sub-type and score. At present, however, the tool is only available for solid tumours.

Source: Authors based on sources cited.

3.2.2. Marketing authorisation and coverage status data were reported as at the end of 2019

81. The data present a cross-sectional snapshot of availability and coverage of medicines *towards the end of 2019* (ranging from 20 September 2019 for Cyprus to 15 January 2020 for Chile)³³. The data reflect regulatory approval (i.e. marketing authorisation) and coverage determinations, and do not take actual utilisation into account. Unfortunately, no data on dates of market launch were collected. Respondents were asked to provide information for each medicine by indication(s) for which it is used (i.e. pembrolizumab for non-small cell lung cancer). The survey did not take into account any coverage restrictions (such as population limits, line of therapy, use alone or in combination, requirements to demonstrate a therapeutic response, prior authorisation or step-therapy requirements etc.) which vary

³³ Note that responses to this part of the survey were incomplete, and as such, data on all indicators are not presented for all respondent countries.

between (and sometimes within) countries. It also did not take into account differences in coverage by treatment setting (dispensed to patients for self-administration, administered in hospitals and ambulatory care settings as part of outpatient services, or administered to hospital inpatients) as countries were permitted to provide only one response for each product/indication pair. It is acknowledged that in some countries, coverage may vary between settings of care.

82. Since 1995, all oncology 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. Through the centralised procedure, medicines are approved in all European Union Member States³⁴ as well as in Iceland, Liechtenstein and Norway. However, having a valid central marketing authorisation does not necessarily mean that a product is or will be marketed in a given country. Additionally, many older medicines marketed prior to the establishment of the EMA may have been authorised at national level, or may have only been approved for a subset of indications. As a result, where a product is classified as "not approved" in one country but "approved" in another, it may mean that 1) it is an older product not approved in all countries, or 2) the product has not been launched on the market in that country, either at all, or for that indication. Examples were reported by several countries including Cyprus, Greece, and Norway, and may explain some of the differences in responses regarding the regulatory approval status of product/indication pairs across EU countries.

83. Country-specific reporting details are presented in Table A B.1 of Annex B. The table outlines limitations of the data, and assumptions made by countries when completing the survey. It also includes dates of survey submission (ranging from 20 September 2019 for Cyprus to 15 January 2020 for Chile), which are relevant since the evolution of approvals and coverage decisions in oncology is rapid. A medicine indicated as "not approved" or "not covered" may in fact be a medicine which is *not yet* approved or covered, or it may be a medicine for which an application for marketing authorisation or (more likely) coverage was rejected.

84. Unless otherwise specified, information on coverage reflects the nationwide coverage status for the product/indication at the time of survey completion. This is the case in all countries in which coverage decisions are made at the national level, and apply to all patients in the country, independent of the setting of care in which the medicine is administered (hospital, ambulatory care, home, etc.). In other countries, the information collected does not necessarily apply to all patients, all care settings, or all regions. In Australia, for example, the information provided only pertains to the Pharmaceutical Benefits Scheme, which provides national-level coverage for medicines supplied in all settings other than the treatment of public hospital inpatients. Decisions on the coverage of medicines administered to public hospital inpatients are taken at regional level and thus vary between Australian states and territories. In Sweden, the information fully reflects nationwide coverage of medicines used in outpatient care but may be less comprehensive for medicines used in inpatient care, for which coverage is determined at regional level. These differences are discussed in section 3.5.

³⁴ Austria, Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, the United Kingdom.

3.2.3. “Time to access” included the entire period between application for marketing authorisation and (national) coverage decision

85. “Time to access” for a medicine (or an indication) is generally measured as the time between submission of the application for marketing authorisation in the country (or region for EU) and the date of the coverage decision.³⁵ Indeed, application for marketing authorisation is the first step to gaining market access, though in many countries, companies may only launch a medicine once it has coverage (often at a regulated price). There are some exceptions; in the United States, Canada, England, and Germany, companies generally launch their products just after the marketing authorisation, either because every medicine authorised is covered by default (England, Germany) or because coverage decisions are made by individual insurers or public plans for their beneficiaries (Canada and the United States).

86. In oncology, two other factors are likely to influence time to access.

- First, in many countries, some patients can gain access to oncology medicines through early access schemes, before the medicine/indication is covered or sometimes before it is approved. Such schemes may be limited to medicines treating severe diseases, for which no effective treatments are available. Oncology products often meet these criteria, making them eligible for early access mechanisms. In addition, where coverage (or inclusion in a positive list) is denied for any reason, in some countries individual patients may be granted exceptional access on request. As these exceptional access schemes that require prior authorisation for individual patients³⁶ are limited in scope, and access to medicines is significantly more complex for prescribers and patients, they are clearly no substitute for general coverage. In this study, early access schemes were not taken into account in the calculation of time to access.³⁷
- Second, even where a new indication for an existing product is not (yet) approved or covered, access may be possible through off-label prescribing. This however, will be subject to the coverage for these prescriptions.

87. In this study, time to access was measured as the time (in months) between the submission of an application for marketing authorisation and a coverage decision (see Figure 3.1). It was decomposed into three periods.

- Period 1 was defined as the time between the date of submission of the application for marketing authorisation and the date of marketing authorisation (i.e. approval). It includes the regulatory agency processing time, including any “clock stops”, i.e. time taken by the company to provide additional information requested by the regulator to inform the assessment of the application. This indicator was calculated for all pairs that were reported as approved.
- Period 2 was defined as the time between the date of marketing authorisation and the date of application for coverage. This information is relevant in countries where a “coverage decision” is made at the national level, less so for others (see Table 3.4, the contents of which will be discussed in section 3.5). In order to accelerate access, some countries, including Australia, Belgium, Cyprus, Estonia, Ireland, and Norway, allow companies to submit applications for coverage before they receive marketing authorisation. In Israel, coverage decisions for the whole country and all care settings are made once a year for all applicants (during October-December), and take effect in January of the following year; in some cases, coverage decisions may also precede formal

³⁵ Noting that, in some countries, there may yet be some time elapsing between the coverage decision and access by patients.

³⁶ Prior authorisation may also be required for medicines in general coverage schemes.

³⁷ In addition, in countries where early access schemes provide access to subsidised medicines, companies may be less eager to conclude price negotiations to obtain general coverage. This may in turn increase “time to access” as measured in this study.

marketing authorisation. This indicator was calculated for all product/indication pairs that were reported as approved and covered.

- Period 3 was defined as the time between the date of application for coverage and the date of coverage decision, which is only relevant for countries where such a process exists at central level and if the medicine is covered. Time to launch, as used in other studies, would have been more informative, but could not be elicited. This indicator was calculated for all pairs that were reported as approved and covered.

Figure 3.1. Time to access as measured in this study

Source: Authors.

3.3. Access to oncology medicines is unequal across OECD/EU countries

88. Access to oncology medicines, as measured by regulatory approval and coverage status, remains unequal across OECD/EU countries. The following sections present the results of the OECD's survey on regulatory approval and coverage status for a selected sample of oncology medicines (as described in Section 3.2), with a breakdown by country, vintage of the medicine, and cancer type. This is followed by a discussion on the results of the OECD survey compared with prior studies, and a small section on shortages of oncology medicines.

3.3.1. Regulatory approval and coverage status varies substantially, with less variation seen for older, essential medicines

89. The proportion of the 109 product/indication pairs in the sample approved (i.e. with a marketing authorisation) and covered varied substantially across OECD/EU countries (Figure 3.2 panel A). The United States reported the largest percentage of product/indications covered (by Medicare), followed by Denmark and Germany (96%, 91%, and 88%, respectively). Chile and Malta reported the smallest

proportion of pairs approved and covered (47% and 46% respectively). Latvia and Hungary had the largest proportion of medicines approved but not (or not yet) covered (43% and 40%, respectively).

90. Access was better and more homogeneous for the 32 product/indication pairs listed on the World Health Organization's 21st *Model List of Essential Medicines* (WHO-EML) (Figure 3.2 panel B). With the exception of Hungary and Australia³⁸, at least 80% of the 32 product/indication pairs were approved and covered in all responding countries.

91. For the 31 newer product/indication pairs, regulatory approval and coverage status varied considerably (Figure 3.2 panel C). In the United States, Germany and Denmark, more than 90% of these newer product/indications were covered, while in Japan, the United Kingdom (England), Switzerland, and Sweden, the figure was 70 to 80%. Other countries had fewer product/indications covered. While in Korea and Chile this is partly explained by the fact that some medicines were not yet approved, in the remaining countries, it is more likely that coverage decisions had not yet been made or coverage was denied.

Figure 3.2. Percentage of sample product/indication pairs by approval and coverage status across OECD/EU countries

A: Based on total sample of 109 product/indication pairs

³⁸ No data for Australia were provided for 7 of the 32 product/indication pairs.

B: Based on sample of 32 product/indication pairs included on the WHO 21st Model List of Essential Medicines

C: Based on sample of 31 product/indication pairs approved by the US Food and Drug Administration since 2014

Note: Data for Australia were not included in panel A and C as many data were missing.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

3.3.2. Differences in approval and coverage are also observed between cancer types

92. Regulatory approval and coverage status of medicines also varied across OECD and EU countries by cancer type (see Table A C.1 to Table A C.6 in Annex C). Respondent countries, on average, approved and covered 77% of products indicated for metastatic breast cancer, 69% for non-small cell lung cancer and colorectal cancer, 62% for melanoma, 75% for multiple myeloma, and 83% for supportive care in oncology, respectively.

93. For the treatment of **metastatic breast cancer**, countries generally reported coverage for at least one medicine in each class of products, with the exception of platinum compounds³⁹ and protein kinase inhibitors, with the latter not covered in Chile or Lithuania (Table A C.1). Most countries covered all WHO-EML medicines. Not surprisingly, newer medicines were less likely to be available because some may have not yet been approved in some countries (Chile, Korea, Switzerland and Japan) and others may not yet have been covered (Chile, Korea, Eastern European countries).

94. Disparities were noted in the coverage of medicines for **non-small cell lung cancer** (Table A C.2). Generally, older medicines and those on the WHO-EML were approved and covered, with the exception of carboplatin, cisplatin and etoposide in some countries. In all countries, at least one protein-kinase inhibitor and one monoclonal antibody were reported as covered, with the exception of Latvia, with no covered monoclonal antibody.

95. Management of **colorectal cancer** often includes fluorouracil, capecitabine, irinotecan and oxaliplatin, all of which are included in the WHO-EML. With the exception of Hungary, all were reported as approved and covered in all countries (Table A C.3). Of the newer medicines, neither nivolumab nor pembrolizumab had marketing authorisation for colorectal cancer in the EU, and were thus not approved for that indication. However, both were indicated as approved and covered in Chile, Israel and the United States.

96. Nivolumab and pembrolizumab are the only two medicines on the WHO-EML indicated for **melanoma**. Both have been approved in the EU or the United States in the last five years, and at least one was reported as approved and covered in all countries (Table A C.4). In addition, at least one drug from the protein-kinase inhibitor class was covered in all countries except Chile. Talimogene laherparepvec is a novel oncolytic immunotherapy for melanoma; of the countries that provided data for this medicine, it was covered only in Switzerland, Germany, Denmark, the United Kingdom (England), and the United States.

97. Nearly every country covered all WHO-EML medicines for **multiple myeloma** (except Latvia, Israel and Hungary) (Table A C.5). There was less disparity in approval and coverage status for the older medicines than in the newer ones. None of the newer medicines for this indication received coverage in Chile, Lithuania, Latvia or Malta; all were covered in Belgium, Denmark, Germany, Japan, and the United States.

98. With regard to medicines used in **supportive care** in oncology, all countries covered calcium folinate and at least one colony-stimulating factor and corticosteroid (Table A C.6).

³⁹ This, however, may be due to a reporting issue. Platinum compounds are old products, approved at national level and their Summary of Product Characteristics does not necessarily specify indications.

3.3.3. Results from the OECD survey are consistent with previous studies

99. These results from the OECD survey are consistent with previous studies on coverage of cancer medicines across countries. The two ESMO studies mentioned previously surveyed the national formulary availability, out-of-pocket costs and accessibility of cancer medicines for solid tumours across 49 European countries in 2014 and 63 non-European countries in 2015 (Cherny et al., 2016^[61]; Cherny et al., 2017^[62]). In Europe, the ESMO study showed differences in availability across countries, particularly for targeted agents approved in the last 10 years, which were not available in countries with lower incomes (e.g. Eastern Europe). Access in Eastern Europe has improved for all cancers included in the OECD survey. Many product/indications that were reported as having no coverage in Eastern European countries in the ESMO survey are now covered (i.e. Czech Republic, Estonia, Hungary, Latvia, and Lithuania). This suggests that availability in such countries may be an issue of the time lag between marketing authorisation, market launch by the manufacturer, and coverage decision. That said, in the ESMO survey, major disparities in national formulary inclusion were observed for medicines to treat melanoma, and this still remains the case. For non-small cell lung cancer, colorectal cancer, and breast cancer, disparities were limited to distinct subgroups of patients (e.g. by disease status). Consistent with the OECD survey, less variation was observed for WHO-EML medicines. Among high-income, non-European OECD countries, most WHO-EML medicines were available. Cancer medicines were least accessible in countries with low incomes.

100. Several studies have evaluated the utilisation of oncology medicines using different metrics. A longitudinal analysis of 31 cancer drugs approved between 2000 and 2012 in three European countries (Belgium, Scotland and Sweden) measured utilisation of the drugs in DDDs per 1000 population between 2008 to 2013 (Ferrario, 2017^[67]). The number of indications and the number of years since EU-wide marketing authorisation were positively correlated with utilisation, while price per DDD and the average rating of clinical added-value across all indications (with a higher score when the added-value was low or zero) were negatively correlated with utilisation.

101. The Swedish Institute for Health Economics *Comparator Report on Cancer in Europe* (2019^[4]) examined the uptake of cancer medicines in seven cancer types (plus immunotherapy) across Europe in 2018. Uptake was measured as the number of standard weekly doses (in mg) per the number of deaths from the cancers for which the medicine was indicated, as the definition of a case. Countries were categorised into three groups based on GDP/capita. The lowest tier included Bulgaria, Croatia, the Czech Republic, Hungary, Latvia, Lithuania, Poland, Portugal, Romania, the Slovak Republic, and Slovenia. The middle tier included the “Big 5” – France, Germany, Italy, Spain, and the United Kingdom. High tier countries were Austria, Belgium, Denmark, Finland, Iceland, Ireland, the Netherlands, Norway, Sweden and Switzerland. Unsurprisingly, the report showed that uptake varied across countries, relating to economic status, with uptake in poorer countries being one third to one half of that of the Big 5 and the wealthier countries. Among the Big 5, France and Germany had the highest level of uptake while the United Kingdom had the lowest across all cancer types and immunotherapy. Among the high-tier countries, Switzerland had a consistently high uptake across all the cancers studied. For breast cancer, uptake of newer medicines other than trastuzumab was slow, with almost no uptake in some countries (e.g. Lithuania). Uptake of medicines for colorectal cancer varied across countries, with some low tier countries having higher utilisation than middle and high tier countries. The most significant differences in uptake observed related to immunotherapy and medicines for multiple myeloma and prostate cancer. Austria, Belgium and Switzerland had the highest uptake of immunotherapy, while Lithuania, Latvia and the Czech Republic had the least. The smallest disparities observed were for lung cancer medicines.

3.3.4. Supply interruptions and shortages also affect access to oncology medicines

102. In addition to marketing authorisation, coverage, and financing, access to oncology medicines may also be impaired by the increasing occurrence of supply interruptions and shortages. To explore this, respondents to the OECD survey were asked whether they had experienced shortages of oncology medicines in the preceding three years, and, if so, to provide more detailed information. Seventeen of 24 respondent countries (71%) reported having experienced shortages, and only four countries reported that they had not experienced shortages (Germany, Japan, Sweden, and Switzerland).⁴⁰ Although the data collected did not allow for further analysis, it was evident that products reported to be in short supply varied between countries, but generally involved older, generic drugs.

103. Several studies report shortages of inexpensive (injectable) cancer medicines as a concern (Cherny et al., 2016^[61]; Vyas et al., 2019^[68]; Acosta et al., 2019^[69]). The forthcoming OECD Health Working Paper *Shortages of Medicines in OECD Countries* further explores the issue of medicine shortages, their possible root causes, and actions implemented to tackle this issue (Shortages of Medicines in OECD Countries, Forthcoming^[70]).

3.4. Time to access for new oncology product/indications varies across OECD/EU countries

104. Times to access were computed for the 31 new product/indication pairs in the sample⁴¹ (method described in Section 3.2). New products and/or indications were reportedly most often first approved in the United States. In individual countries/regions, approval occurred on average across the sample 12 to 17 months after first marketing authorisation in the sample of countries surveyed. Coverage decisions were typically made a few months later, with total time from first approval of up to 66 months. Time between marketing authorisation and coverage decision also varied across OECD/EU countries, reflecting different regulatory, health technology assessment (HTA), coverage and pricing processes.

3.4.1. On average, new product/indications are approved in OECD/EU countries 12 to 17 months after the first country marketing authorisation

105. Among 31 new product/indication pairs in the sample approved since 2014, 26 obtained their first marketing authorisation in the United States, while 4 were first approved in Japan and 1 in Switzerland (see Table 3.2). Table 3.2 shows the elapsed time between date of first marketing authorisation (out of the sample countries) and marketing authorisation in subsequent countries/regions for each product/indication pair. All European countries except Switzerland have been grouped into the European Economic Area (EEA)⁴², as marketing authorisation is centralised for oncology products.

106. Market launch sequences varied for each product/indication pair in the sample. In individual countries/regions, approval occurred on average across product/indications 12 to 17 months after first marketing authorisation in the sample of countries surveyed (range 2 to 52 months for individual pairs). This reflects both patterns arising from companies' launch strategies and the duration of the regulatory process. The latter is likely to be longer for initial approvals of new medicines than for subsequent extensions of indications.

⁴⁰ The three remaining countries did not respond to the question.

⁴¹ Note that each time period indicator could not be computed for all countries who responded to Part 3 of the OECD survey as necessary data may not have been provided.

⁴² The European Economic Area (EEA) includes EU countries and also Iceland, Liechtenstein and Norway.

Table 3.2. Time between first marketing authorisation and marketing authorisation in subsequent countries/regions for product/indications approved since 2014 (n=31 pairs)

Indication	Active substance	First marketing approval		Time since first marketing approval and subsequent approval in each country/region in months (number of pairs approved, with information on dates ¹)						
		Country	Date	USA (31)	EEA (29)	JPN (25)	ISR ² (20)	CHE (25)	KOR (21)	CHL (9)
Metastatic breast cancer	abemaciclib	USA	Sep-17	0	12	12	15	20	20	27
	olaparib	USA	Dec-14	0	52	43	b	13	8	a
	palbociclib	USA	Feb-15	0	21	31	b	23	18	b
	ribociclib	USA	Mar-17	0	5	a	b	7	a	b
	talazoparib	USA	Oct-18	0	8	a	a	a	a	a
Non-small cell lung cancer	alectinib	JPN	Sep-15	3	17	0	7	16	13	c
	atezolizumab	USA	May-16	0	16	20	13	12	8	9
	brigatinib	USA	Apr-17	0	19	a	19	a	19	a
	ceritinib	USA	Apr-14	0	13	23	13	16	9	8
	dacomitinib	USA	Sep-18	0	7	4	a	11	a	a
	durvalumab	USA	May-17	0	16	14	9	13	19	a
	lorlatinib	JPN	Sep-18	2	8	0	a	a	a	a
	necitumumab	USA	Nov-15	0	3	43	17	a	a	a
	nivolumab	USA	Dec-14	0	10	12	3	11	3	12
	osimertinib	USA	Nov-15	0	3	4	6	8	6	31
	pembrolizumab	USA	Oct-15	0	9	14	c	16	c	c
	ramucirumab	USA	Apr-14	0	21	26	25	9	12	12
Colorectal cancer	nivolumab	USA	Dec-14	0	a	a	3	11	3	12
	pembrolizumab	USA	Sep-14	0	a	51	5	29	6	a
	ramucirumab	USA	Apr-14	0	21	25	25	18	12	12
	trifluridine / tipiracil	JPN	Mar-14	18	25	0	a	41	a	a
Melanoma	binimetinib	USA	Jun-18	0	3	7	a	a	a	a
	cobimetinib	CHE	Aug-15	3	3	a	10	0	3	8
	encorafenib	USA	Jun-18	0	3	7	b	a	a	a
	nivolumab	JPN	Jul-14	5	11	0	8	16	8	b
	pembrolizumab	USA	Sep-14	0	10	24	5	29	6	b
	talimogene laherparepvec	USA	Oct-15	0	2	a	28	9	a	a
Multiple myeloma	daratumumab	USA	Nov-15	0	6	22	14	13	24	b
	elotuzumab	USA	Nov-15	0	6	10	10	13	12	b
	ixazomib	USA	Nov-15	0	12	16	9	15	20	a
	panobinostat	USA	Feb-15	0	6	5	a	10	24	b
Average length of time per country/region for pairs studied				1	12	17	15	15	12	15
Median length of time per country/region for pairs studied				0	10	14	13	13	12	12

Note: a = product/indication pair not approved (or not launched); b = product/indication pair approved but marketing authorisation date not provided; c = no data provided for that product/indication pair; grey shading = first country marketing authorisation (out of the sample countries) All European countries except Switzerland have been grouped as marketing authorisation in the European Economic Area (EEA) is centralised for oncology products. Australia did not provide data on dates.

1. Israel and Chile provided information on dates only for a subset of product/indication pairs indicated as "approved and covered"

2. For products with several indications, data represent product-level dates only. Indication-specific dates are not available.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

107. Former studies used sales data to estimate time elapsed between first global launch and launch in a given country. Varol et al. (2012^[71]) estimated the time between first global launch and launch in 20 individual countries, for several cohorts of products. The study found a reduction of the median time from four years for medicines launched in 1984-1995 to two years for medicines launched in 1995-2008. In the latter period, medicines were launched first in the United States, then in Germany, the United Kingdom and the other three big European markets (France, Italy, Spain), and finally in Japan. The reduction in launch delays was explained by the creation of the EMA and convergence in regulatory requirements among OECD countries (Varol, Costa-Font and McGuire, 2012^[71]).

108. Cooperation and convergence between regulatory authorities has increased in the past years and new initiatives may further accelerate access (OECD, 2018^[72]). The Orbis project, an initiative by the US FDA, provides a framework for concurrent submission and review of oncology products among international partners. The first review through this process involved regulatory agencies from Australia, Canada and the United States, and led to the simultaneous approval of the use of combination immunotherapy for a particular form of endometrial cancer.⁴³ Each country defines the terms of approval. For this specific product/indication, Australia granted a provisional approval and Canada a conditional approval, both of which require the provision of further confirmatory evidence.⁴⁴ Although to date it has only been applied to “supplemental indications” in oncology, this collaboration has the potential to support more rapid access for patients in the countries involved. However, it does not guarantee that any new indication will be covered and affordable for patients.

3.4.2. Time from first country marketing approval to coverage in a given country ranges from 1 to 66 months

109. In individual countries/regions, coverage occurred on average across product/indications 10 to 56 months after first marketing authorisation in the sample of countries surveyed (range 1 to 66 months for individual pairs). (See Table 3.3). For example, the average time across all indications ranged from 10 months in Israel, followed by 17 months in Japan, to 56 months in Malta (where only 2 product/indications were covered at time of reporting)⁴⁵. This time difference is partly a result of company launch strategies, which determine when marketing approval is sought and the time taken to apply for coverage, where applicable. However, it also reflects differences between countries in the time taken to complete coverage and pricing processes, where relevant.

⁴³ Both medicines were already approved in other indications.

⁴⁴ <https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis>; <https://www.tga.gov.au/media-release/provisional-application-receives-approval-through-first-international-collaborative-review-initiative-between-tga-fda-and-hc>, consulted on 18 March 2020

⁴⁵ Time to access could not be computed for a number of countries that did not provide the necessary information, including Australia, Chile, Germany, Lithuania, and the United States.

Table 3.3. Time between first marketing authorisation and granting of coverage in subsequent OECD/EU countries for product/indications approved since 2014 (n=31 pairs)

Indication	Active Substance	First marketing approval		Time since first marketing approval and subsequent granting of coverage in each country in months (number of pairs approved and covered, with available information on date of coverage decision ¹)																
		Country	Date	BEL (18)	CYP (8)	CZE (12)	EST (12)	FRA (17)	GBR (20)	GRC (12)	HUN (8)	IRL (18)	LVA (4)	MLT (2)	NOR (17)	SWE (19)	CHE (23)	ISR ² (20)	JPN (24)	KOR (10)
Metastatic breast cancer	abemaciclib	USA	Sep-17	21	b	b	b	17	17	b	b	b	a	b	24	21	22	16	14	b
	olaparib	USA	Dec-14	b	b	b	b	b	b	b	b	b	a	b	b	b	20	13	43	b
	palbociclib	USA	Feb-15	34	38	b	55	37	34	40	44	40	b	b	42	28	25	35	33	33
	ribociclib	USA	Mar-17	17	13	b	30	c	9	15	19	23	25	b	13	10	27	10	a	a
	talazoparib	USA	Oct-18	b	a	b	b	b	b	b	b	a	b	b	b	b	a	a	a	a
Non-small cell lung cancer	alectinib	JPN	Sep-15	29	b	48	b	35	35	b	37	26	b	b	33	26	23	4	2	25
	atezolizumab	USA	May-16	22	b	b	42	33	c	b	29	34	b	b	21	21	14	8	23	20
	brigatinib	USA	Apr-17	b	b	b	b	b	23	b	b	26	b	b	30	20	a	9	a	24
	ceritinib	USA	Apr-14	32	b	64	56	31	26	22	b	32	b	b	52	20	41	9	25	28
	dacomitinib	USA	Sep-18	b	b	b	b	b	11	b	b	14	b	b	14	9	b	a	5	a
	durvalumab	USA	May-17	24	b	b	30	b	24	b	b	b	b	b	29	20	16	8	15	b
	lorlatinib	JPN	Sep-18	b	b	b	b	b	b	b	b	13	b	b	b	12	a	a	2	a
	necitumumab	USA	Nov-15	b	b	b	b	b	c	b	b	a	b	b	a	b	a	b	b	a
	nivolumab	USA	Dec-14	25	33	39	b	52	35	c	46	45	b	53	36	38	16	1	12	32
	osimertinib	USA	Nov-15	13	26	38	40	44	12	15	b	b	b	b	b	46	33	2	6	25
	pembrolizumab	USA	Oct-15	c	26	40	38	19	15	16	d	30	b	b	11	28	23	d	16	d
	ramucirumab	USA	Apr-14	b	b	b	b	b	c	b	b	a	b	b	b	c	23	b	26	b
Colorectal cancer	nivolumab	USA	Dec-14	a	a	a	a	a	a	a	a	a	a	a	a	a	16	1	a	b
	pembrolizumab	USA	Sep-14	a	a	a	a	a	a	a	a	a	a	a	a	a	60	4	51	b
	ramucirumab	USA	Apr-14	b	b	b	b	31	b	b	b	b	b	b	b	c	23	b	25	b
	trifluridine / tipiracil	JPN	Mar-14	43	b	42	66	42	29	45	b	35	57	b	41	30	43	a	2	a
Melanoma	binimetinib	USA	Jun-18	17	a	b	b	14	8	b	b	11	b	b	15	9	a	a	8	a
	cobimetinib	CHE	Aug-15	28	b	34	b	18	c	18	38	32	34	b	c	b	9	17	a	b
	encorafenib	USA	Jun-18	17	a	b	b	14	8	b	b	11	b	b	15	9	a	7	12	a
	nivolumab	JPN	Jul-14	21	22	29	28	29	19	19	28	39	b	58	16	33	21	6	2	43

Indication	Active Substance	First marketing approval		Time since first marketing approval and subsequent granting of coverage in each country in months (number of pairs approved and covered, with available information on date of coverage decision ¹)																
		Country	Date	BEL (18)	CYP (8)	CZE (12)	EST (12)	FRA (17)	GBR (20)	GRC (12)	HUN (8)	IRL (18)	LVA (4)	MLT (2)	NOR (17)	SWE (19)	CHE (23)	ISR ² (20)	JPN (24)	KOR (10)
Melanoma (cont.)	pembrolizumab	USA	Sep-14	20	20	40	26	28	13	17	26	21	48	b	14	31	36	4	29	41
	talimogene laherparepvec	USA	Oct-15	b	a	b	b	b	11	b	b	b	b	b	b	b	26	b	a	a
Multiple myeloma	daratumumab	USA	Nov-15	c	33	45	36	43	28	18	c	29	b	b	23	c	19	14	24	41
	elotuzumab	USA	Nov-15	22	b	34	b	b	b	b	b	b	b	b	b	b	21	14	12	b
	ixazomib	USA	Nov-15	23	b	39	b	35	27	25	b	37	b	b	b	30	29	14	18	b
	panobinostat	USA	Feb-15	22	b	b	37	b	23	24	b	b	b	b	47	b	b	a	6	b
Average length of time per country for pairs studied				24	26	41	40	31	20	23	33	28	41	56	27	23	25	10	17	31
Median length of time per country for pairs studied				22	26	40	38	31	20	19	31	29	38	54	24	21	23	9	15	30

Note: a = product/indication pair not approved (or not launched); b = product/indication pair approved but not covered; c = product/indication pair approved and covered but no information on date; d = no data provided for that product/indication pair.

Australia, Chile, Denmark, Germany, Lithuania and the United States did not provide sufficient data to calculate this time difference. In Israel, coverage decisions are made once a year (during October-December) for the whole country and all care settings, and take effect in January of the following year. In some cases, coverage decisions may precede formal marketing authorisation.

1. Belgium, France, the United Kingdom (England), Greece, Hungary, Norway, and Sweden provided information on dates only for a subset of all pairs indicated as “approved and covered”.

2. For products with several indications, data represent product-level dates only. Indication-specific dates are not available.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

3.4.3. Time from application for marketing authorisation to coverage decision varies across OECD/EU countries

110. For a few countries, available information enabled decomposition of the time between dates of marketing authorisation and coverage decisions for approved product/indications in the same jurisdiction. The total time was decomposed into 3 periods: time between application for marketing authorisation and approval (period 1); time between marketing authorisation and application for coverage (period 2); and time between application and coverage decision (Period 3) (see Figure 3.3, and Figure 3.1 for the definition of periods). The following sections discuss the results for each of these periods in turn, followed by the total time between application for marketing authorisation and coverage decision (i.e. periods 1 to 3).

Period 1: Time between application for marketing authorisation and approval

111. The average time between application for marketing authorisation and approval (Period 1) varied across the 5 countries/regions that provided data, with the shortest period being 7 months in the United States, followed by 8 months in Chile, 10 months in Israel and Japan, and 13 months in the European Economic Area (see Figure 3.3 panel A). Observed time differences were longer than the maximum time allowed by the regulator to process an application for marketing approval, as the data included “clock-stops”, and thus cannot be considered regulatory processing times.

112. Previous studies have examined the time between application and marketing approval across countries. For 29 cancer drugs approved by the EMA between 2006 and 2011, one study looked at approval times in three major jurisdictions. Median approval time was shorter in the United States (6.0 months) than in Japan and Europe (15.0 and 13.3 months respectively). While the time difference between the United States and Japan was not explained, the difference between the EU and the United States was attributed to “clock stops” and to the time taken by the European Commission to make a decision after a positive opinion from the CHMP (Hartmann, Mayer-Nicolai and Pfaff, 2013^[73]). Another study, focusing on 16 tyrosine kinase inhibitors (TKIs)⁴⁶ approved by the US FDA as of 30 September 2012, shed some light on the factors influencing the differences in average time spent on review and approval between the United States (205.3 days) and the EU (409.6 days) (Shah, Roberts and Shah, 2013^[74]). The active review time was similar in both jurisdictions, 205.3 days in the United States and 225.4 days in the EU, with the differences attributed to longer clock stops during the review process to collect additional information from applicants, and the time from recommendation by the CHMP, an EMA’s expert advisory opinion, and the decision of the European Commission. These factors also contributed to the longer approval time in the EU found in the aforementioned study by Hartmann, Mayer-Nicolai and Pfaff (2013^[73]).

113. Additionally, for 37 cancer medicines approved between 2005 and 2013 by Health Canada, the time from date of submission to approval was much longer for the EMA and Health Canada than for the FDA, by an average of 6.7 months and 6.4 months, respectively (Samuel and Verma, 2016^[75]). The differences were attributed to the more frequent use of expedited review processes in the United States, as well as differences in administrative procedures applying in the EU. Submissions to the FDA were also made on average 12.9 and 28.4 months earlier than submissions to Health Canada and to the EMA, respectively.

114. A more recent study showed that the overall median approval time for cancer medicines and immunomodulators varied across six major regulatory agencies in the EU, the United States, Japan, Canada, Switzerland, and Australia, from 240 days (the FDA) to 423 days (the EMA and Swissmedic) in 2014-2018 (The Centre for Innovation in Regulatory Science (CIRS), 2019^[76]).

⁴⁶ For these 16 TKIs, 19 applications were approved in total during the period. Review time was only computed for first applications. It would be shorter if computed for all applications.

Period 2: Time between marketing authorisation and application for coverage

115. The time between marketing authorisation (i.e. approval) and application for coverage in the same jurisdiction (Period 2) varied across countries (see Figure 3.3 panel B). This period is often interpreted as a reflection of companies' launch strategies, which may in turn be influenced by national pharmaceutical policies. For example, in some countries, application for coverage may be made prior to the receipt of marketing authorisation of the product for a specific indication (e.g. in Australia, Belgium, Ireland, Norway). This may shorten or even negate the duration of Period 2 for some products. In the sample of countries considered, Ireland had the shortest average time between marketing authorisation and application for coverage (one month), followed by Belgium, and Hungary. Malta had the longest delay, 18 months (computed on the only 2 product/indications covered at the time of reporting).

Period 3: Time between application and coverage decision

116. The time between application and coverage decision (Period 3) is influenced by HTA processes and mechanisms to determine coverage and pricing⁴⁷, and varied on average from 4 months in Sweden to 27 months in Malta (see Figure 3.3 panel C). In Sweden the short time difference may be explained in part by the fact that coverage decisions are made at the product level and not for individual indications, which means that all subsequent indications are covered automatically once the initial indication is covered. Observed delays are in many cases longer than the six-month maximum for EU countries set by the Transparency Directive.⁴⁸ However, in this study, the time measured includes "clock-stops", and cannot be interpreted as administrative processing time.

117. The survey results are generally aligned with those of the European Federation of Pharmaceutical Industries and Associations (EFPIA) Patient WAIT Indicator 2018 survey, with the exception of Hungary, the United Kingdom and Sweden (IQVIA, 2019^[77]). The WAIT indicator computed lags between marketing authorisation and national coverage (Periods 2 and 3) for 31 oncology products granted EMA approval for a new active substance between 1 January 2015 and 31 December 2017, with a cut-off date for coverage of 19 December 2018. Some differences between the two studies remain to be elucidated, but there are at least two reasons for different results. EFPIA used a product-based sample while the OECD survey included product/indications over a different period of time. In the OECD survey, the number of product/indications for which the time difference was computed varied across countries, with a maximum of 31 pairs.

⁴⁷ These mechanisms have been described elsewhere, for example in (Panteli et al., 2016^[97]) or in country profiles available here <https://ppri.goeg.at/publications>, consulted on 18 March 2020, and here <https://www.oecd.org/health/health-systems/Pharmaceutical-Reimbursement-and-Pricing-in-Germany.pdf>, consulted on 08 October 2020.

⁴⁸ EU's Transparency Directive (Council Directive 89/105/EEC), available here: https://ec.europa.eu/growth/sectors/healthcare/competitiveness/products-pricing-reimbursement/transparency-directive_en, consulted on 18 March 2020.

Figure 3.3. Time between application for marketing authorisation and coverage decision across OECD/EU countries, decomposed and aggregate

A: Application for marketing authorisation and approval (Period 1)

B: Marketing authorisation and application for coverage (Period 2)

C: Application for coverage and coverage decision (Period 3)

D: Application for marketing authorisation and coverage decision (sum of Periods 1, 2, and 3)

Note: ♦ average time; + maximum time; - minimum time; grey bars represent the number of product/indication pairs for which the time difference was computed for each country, with the maximum possible being 31 pairs. Times elapsed were not computed for all 23 countries who responded to the survey due to missing date information. In Israel, for products with several indications, data represent product-level dates only. Indication-specific dates are not available. Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Period 1 to 3: Total time between application for marketing authorisation and coverage decision

118. Given the variations observed in the decomposed periods, it is not surprising that disparities were evident in the aggregate times between application for marketing authorisation and granting of coverage (the sum of Periods 1, 2, and 3). Times ranged from 9 and 11 months on average in Israel and Japan respectively, to 52 months in Malta (see Figure 3.3 panel D). As noted previously, in Israel coverage decisions are made only once a year (during October-December), and take effect in January of the following year. Japan reported the shortest time between marketing authorisation and coverage decision (i.e. Periods 2 and 3), an average of two months. In Japan, coverage of a new medicine generally commences within 60 days (or 90 days at the latest) from the time of approval. The reimbursement process starts immediately after approval of the medicine, and additional indications are covered by health insurance from the day of approval. Prices are not negotiated with companies; reimbursement prices are set by the government.

3.5. Countries report inequities in access and difficulties in meeting patient expectations

119. Half of the 24 respondents to the policy questionnaire confirmed that inequities in access exist within their countries.⁴⁹ These inequities vary in nature and extent, and may be due to differences in coverage across regions, health care settings or population groups as well as cost-sharing policies.

3.5.1. Pharmaceutical coverage is not always uniform within countries

120. Inequity of access within countries may arise from non-uniform coverage across regions or population groups. While most OECD and EU countries make coverage decisions at the national level, some countries take more decentralised approaches (see Table 3.4). In some countries, funding of cancer medicines, including inpatient and outpatient treatment, is a regional or even municipal responsibility, and coverage decisions are made at this level. This is the case in some Nordic countries, for example. Local or regional administrations may have variable capacity—both administrative, technical and financial—to respond to the pressures that cancer medicines pose to their systems. In some countries, health care coverage is provided by different entities (national and sub-national governments, private health insurers, etc.), with differences in the content of formularies⁵⁰, conditions of access, and the type and level of co-payment. This can all create significant disparities in access across populations.

121. In Australia, the Pharmaceutical Benefits Scheme (PBS) provides national coverage for medicines supplied in the community and to hospital outpatients. Under the National Health Reform Agreement, the Australian Government also contributes to the delivery of public hospital services including the provision and funding of pharmaceuticals, however hospital formulary selection is a matter for states and territories and may take place at state, regional or institutional level.

122. In Canada, access to oncology medicines is non-uniform across provinces and territories, and inequity in access is a frequent topic of public discourse (Chafe et al., 2011^[78]). The federal government makes coverage decisions at the national level for certain groups of Canadians covered by federal public plans (members of the Canadian armed forces, veterans, First Nations peoples living on reserves, Inuit people in northern communities, certain classes of immigrants and refugees, and persons incarcerated in the federal correctional system). Provincial governments make coverage decisions for those residents that

⁴⁹ Canada, Chile, Denmark, Ireland, Israel, Italy, Latvia, Malta, Norway, Sweden, Switzerland, the United States.

⁵⁰ A formulary is a list of medicines covered by a specific coverage scheme. The term is also used in hospitals for the list of medicines available to prescribers.

qualify for public plans, and for all inpatient medicines. Individual private insurers make decisions on medicines used in outpatient care for their enrollees. Public coverage of outpatient drugs is usually linked to patient age and/or income, but only accounts for roughly 40% of retail pharmaceutical expenditure. In 2011, the pan-Canadian Oncology Drug Review (pCODR) was introduced to address uneven coverage and lack of transparency in provincial review processes of cancer medicines in Canada. The pCODR assesses clinical evidence and cost-effectiveness of new cancer medicines in order to make recommendations to the provinces and territories (McDonald et al., 2016^[79]). These recommendations guide the allocation of publicly funded resources. Ultimately, however, coverage depends on the willingness of the province or territory to consider a product for listing. With resource limitations, provinces and territories must inevitably make choices, taking into account local opportunity costs (McDonald et al., 2016^[79]). Nevertheless, since the implementation of pCODR, there has been greater concordance among provinces in cancer drug funding decisions, and the time to decision has been reduced (Srikanthan et al., 2017^[80]).

Table 3.4. Level of coverage decision making across OECD/EU countries

Level of coverage decision making for medicines	Country
<i>Dispensed to patients for self-administration</i>	
National	AUS, BEL, CAN (Federal public plans), CHE, CYP, DEU, EST, FRA, GBR, GRC, HUN, IRL, ISR, ITA, JPN, KOR, LVA, LTU, NOR, SWE
State/Provincial	AUS, CAN (Provinces & Territories' public plans), USA (Medicaid)
Regional	AUS, DNK, ITA, NOR ¹
Municipal	
Individual health coverage schemes	CAN (private insurance), ISR, USA (private plans, Medicare part D)
Insurer-provider network	ISR
Other	
<i>Administered in hospitals or ambulatory care settings as part of outpatient care services</i>	
National	AUS, BEL, CAN (certain groups), CHE, CYP, DEU ² , EST, FRA, GBR, GRC, HUN, IRL, ISR, ITA, JPN, KOR, LVA, LTU, NOR, USA (Medicare Part B)
State/Provincial	AUS, CAN (public plans)
Regional	AUS, BEL (for prevention products), DNK, ITA, SWE, USA
Municipal	IRL, LTU
Individual health coverage schemes	CAN, IRL, ISR
Insurer-provider network	
Other	
<i>Administered in hospitals during inpatient stays</i>	
National	AUS (private hospitals), BEL, CAN (certain groups), CHE, CYP, DEU ³ , EST, FRA, GBR, GRC, HUN, IRL, ISR, ITA, JPN, KOR, LVA, LTU, NOR, USA (Medicare part A)
State/Provincial	AUS (public hospitals), CAN (Provinces & Territories' public plans)
Regional	AUS (public hospitals), DNK, ITA, SWE
Municipal	IRL, LTU
Individual health coverage schemes	IRL, ISR
Insurer-provider network	CHE
Other	USA

Note: 1. Although coverage decisions are a competency of regions, the four Regional Health Authorities have delegated this responsibility to a Decision Forum, which makes decisions de facto national. Multiple options are possible per setting of care. 2. In general, all products administered in hospitals and ambulatory care settings as part of outpatient care services are covered. 3. The national representation of sickness funds makes coverage decisions for inpatient medicines for all people in statutory health insurance.

Source: Authors, based on 2019 OECD survey on challenges in access to oncology medicines.

123. In some countries in which coverage decisions are decentralised, recent initiatives have promoted more uniform coverage. In Norway, coverage decisions for hospital drugs (all oncology treatments) are devolved to the four Regional Health Authorities, but they have delegated this responsibility to a Decision Forum, whose decisions are *de facto* national. In Italy, where positive lists exist at both the national and regional levels, innovative medicines (not limited to oncology) must be included in all regional lists, in order to reduce regional variations.

124. In the United Kingdom (England), NHS England and NHS Improvement support the national commissioning of cancer medicines according to national service specifications. Decisions on the delivery setting (self, direct general hospital, tertiary hospital) fall outside marketing authorisation and coverage decisions. As such, NHS England's policies set out pathway arrangements, and the associated impact assessments provide information on the delivery setting and prices of both drugs and their administration.

125. In the United States, the complexity of the health care system gives rise to significant variation in patient access according to the type of insurance, the products covered, and the magnitude of out of-pocket costs. Under Medicare, self-administered drugs are covered under Medicare Part D. Plans that contract with Medicare Part D are authorised to determine whether products are reasonable and necessary for the diagnosis or treatment of an illness or injury, subject to certain statutory and regulatory limits. Formulary design must be adequate and non-discriminatory, and formulary plans must be reviewed and approved by Centers for Medicare & Medicaid Services (CMS). Oncology medicines nevertheless belong to one of several "protected classes", for which Medicare Part D plans are required to cover *all* medicines. For medicines administered in hospital and physician settings (covered under Medicare part B), national coverage determinations for medicines are very rare, but are made occasionally. Such coverage decisions are usually made by private regional contractors, based on general non drug-specific national instructions. Hospitals generally decide what products are used for inpatients through a hospital committee. Medicare payment to hospitals is typically provided as a lump sum on the basis of diagnosis, and is not decomposed into different components of treatment of a particular illness or injury. Note that as available insurance plans vary from state to state, regional differences may also play a role in disparities in access across the United States.

126. Other factors may create differences in access within and across countries. For example, Ireland and Chile reported differences in the coverage of oncology medicines and cancer care between patients with private and public health insurance. Additional factors include regional differences in prices and inconsistent policies across service delivery settings within a health care system, as well as differences in purchasing power, procurement processes, and ability and willingness to pay. Geographic variations may also arise due to limited access to prescribers and cancer centres in rural and remote areas (e.g. Australia, Chile).

3.5.2. Meeting patient expectations for access can be challenging

127. The final issue elicited in the preliminary discussions was the challenge of meeting patient expectations for timely access to new and promising medicines. Twenty⁵¹ of the 24 respondents to the survey (83%) reported that concerns about access to oncology treatments, affordability, and sustainability had been raised in public position statements or in the media. With the recent uptick in the number and speed at which new oncology medicines (and new indications) have gained marketing authorisation, there is increasing pressure on HTA agencies and payers to assess these and make coverage decisions. HTA agencies/payers may thus need to prioritise among a number of cancer medicines which to evaluate and consider for coverage first. The arrival of competing products launched within a short time span adds to the pressure, though it can also present potential opportunities for payers. One approach several countries

⁵¹ Australia, Belgium, Canada, Denmark, Estonia, France, Germany, Hungary, Ireland, Israel, Italy, Korea, Latvia, Lithuania, Malta, Norway, Sweden, Switzerland, the United Kingdom (England only), the United States.

have adopted to address patient expectations around access to oncology medicines is to involve patients or patient groups in the HTA process, in one capacity or another, as has been done in Australia, France, Ireland, Lithuania, Norway, Sweden, Switzerland, and the United Kingdom (England).

128. While it is desirable to facilitate rapid access to treatments for sub-populations of patients who might otherwise have no or limited treatment options, it must be acknowledged that introducing medicines with limited evidence of efficacy or effectiveness may in some circumstances put patients at risk and generate excess costs to the health care system.

3.6. Cost-sharing and medicine prices affect affordability

129. In most OECD countries, the entire population is covered for a core set of health products and services, which generally includes medicines. There are few exceptions: 8.5% of the population was uninsured in the United States in 2018, around 7.5% in Poland, and between 5% and 6% in Chile, the Slovak Republic, Estonia, and Hungary (Berchick, Barnett and Upton, 2019^[81]; OECD, 2019^[82]). In Canada, Medicare does not include coverage for prescription medicines and the extent of public coverage is determined at provincial level.

130. Even when covered, patients may face significant user charges or cost-sharing requirements when accessing services and products covered by third parties. These can constitute a substantial barrier to access or cause financial distress to patients and their families. The situation is seen as so critical in some countries that it has led to the coining of the term “financial toxicity”, which the US National Cancer Institute defines as⁵²:

In medicine, a term used to describe problems a patient has related to the cost of medical care. Not having health insurance or having a lot of costs for medical care not covered by health insurance can cause financial problems and may lead to debt and bankruptcy. Financial toxicity can also affect a patient's quality of life and access to medical care. For example, a patient may not take a prescription medicine or may avoid going to the doctor to save money. Cancer patients are more likely to have financial toxicity than people without cancer. Also called economic burden, economic hardship, financial burden, financial distress, financial hardship, and financial stress.

131. User charges are often uniform or very similar in countries where health benefits are defined centrally, even though exemptions or reduction of cost-sharing requirements may apply for specific population subgroups, such as children or low-income populations. In the United States, both benefits covered and cost-sharing requirements vary widely across the various public and private health coverage schemes.

3.6.1. Cost-sharing requirements can compromise access or cause financial toxicity

132. The OECD survey collected information on cost-sharing requirements for three categories of goods and services involving the use of oncology medicines, with the objective of producing a qualitative assessment of coverage beyond the dichotomous coverage status of individual medicines. Three types of information were collected:

- The type and the level of cost-sharing (see Box 3.2 for definitions) for each category of care (medicines dispensed to patients for self-administration; outpatient specialist cancer services including the administration of a medicine; hospital inpatient care for cancer including the administration of a medicine);)

⁵² See <https://www.cancer.gov/about-cancer/managing-care/track-care-costs/financial-toxicity-pdq>, consulted on 18 March 2020.

- Where relevant, the existence of exemptions or reductions in co-payments for some population groups (e.g. children, low-income, patients with certain diseases);
- Information on the existence of a cap on user charges.

Box 3.2. Types of user charges or cost-sharing requirements - definitions

Payments by patients at the point of care to contribute to covering the cost of care, commonly referred to as “user charges”, “cost-sharing requirements” or “cost-sharing arrangements” can take many forms. In this report, they are defined as follows:

- **Co-insurance:** the insured person pays a share of the cost of the medical service (e.g. 10%);
- **Co-payment:** fixed amount) paid by an insured individual for the consumption of a healthcare service (e.g. per hospital day, per prescription item);
- **Deductible:** fixed threshold below which an insured person must pay the full cost of health goods and services out-of-pocket before insurance coverage begins. It is defined for a specific period of time: one year, one quarter or one month. Deductibles can apply to a specific category of care (e.g. doctors' visits, pharmaceutical spending) or to all health expenditures (general deductible).
- **Extra-billing:** refers to any difference between the price charged by a provider and the price covered by the applicable insurance or health coverage scheme. Extra-billing exists, for example, where medical practitioners are allowed to charge fees beyond a negotiated fee paid by a third party. In some countries such as Australia, this is referred to as a “gap payment” for a professional service. In the pharmaceutical sector, where “reference prices” are often used, a fixed reimbursement amount is set for a cluster of products, while sellers remain free to charge a higher price. The patient pays out-of-pocket any difference between the price of a medicine and the reference price.
- **Safety net:** refers to thresholds beyond which a person (or family) may receive prescription medicine items at lower cost or at no cost (e.g. Australia, see Annex D). In some countries, these are referred to as “stop-loss provisions”.
- In many countries, patients may face several types of user charges, for instance the combinations of a deductible or co-payment or co-insurance.

In the OECD/Eurostat/WHO System of Health Accounts (2017^[83]), **out-of-pocket costs or expenditures** include user charges but also expenditures for goods and services not covered at all.

Source: (Auraaen et al., 2016^[84]) and (OECD/Eurostat/WHO, 2017^[83])

133. In oncology, where medicine prices can be very high, cost-sharing requirements can significantly affect affordability for patients. Based on the information from the survey (see Table A D.1 in Annex D), countries were categorised according to the type of cost-sharing applied to cancer care, along a gradient of increasing financial burden (see Figure 3.4 to Figure 3.6). Fixed co-payments, which do not increase with the price of the medicine, create a more predictable and regulated financial contribution than co-insurance. More broadly, affordability is improved when vulnerable populations are protected by lower and capped cost-sharing or exempted from it altogether.

134. Results from the OECD survey are presented below, by setting of care in which medicines are provided:

- In 13 countries, patients can access oncology medicines dispensed for *self-administration* free of charge at the point of care or with a low fixed co-payment (see Figure 3.4). This is the case for example in Australia, where patients have to pay up to a maximum co-payment of AUD 41.00 per prescription item, with the amount reduced to AUD 6.60 for vulnerable population. In 10 countries, patients are required to pay a share of the costs – from 10% in Switzerland to 30% in Japan. In Germany, there is co-insurance of 10% of the cost of a medicine but capped at EUR 10 per item. In some countries, oncology treatments have lower cost-sharing than other medicines. For example, in Belgium and France, oncology medicines carry no co-insurance. In England patients

do not pay anything for oncology treatment, while there are prescription fees for other types of medicines.

- In most responding countries, *outpatient cancer care services* are free of charge, at least when delivered by public providers (see Figure 3.5). Where public providers are available, affordability for patients is not an issue in these countries. Patients in Switzerland, Korea, Japan and the United States are required to pay co-insurance amounts for these services (respectively 10%, 5%, 30% and around 20% in typical health plans).
- The situation is very similar for *inpatient cancer care*, except that in many cases, patients must also pay fixed co-payment per day for accommodation (see Figure 3.6).

135. Many countries apply caps on user charges, either for the category of care or for the total user charges accumulated in one year. Caps may be expressed as fixed amounts of out-of-pocket payments (e.g. Australia, Denmark) or as a share of household income (e.g. Germany). Caps commonly represent around 1% of the average wage in European countries, while they can exceed 9% in the United States and 10% in Korea.

Figure 3.4. Cost-sharing for oncology medicines dispensed to patients for self-administration in OECD/EU countries

Note: This figure does not take into account potential user charges linked to the use of “reference prices”.

1. In Cyprus, people earning less than EUR 135 000 do not share the costs. Beyond this limit, they pay the full cost of care. 2. Belgium and France have co-insurance for some other medicines, but no co-insurance for oncology medicines. 3. In Ireland, there is a fixed co-payment for Medical Card Holders, with deductible for other groups. 4. In Hungary, there is a co-payment of HUF 300 per pack for self-administered products. 5. In Denmark, Sweden, and Switzerland there is a deductible before co-insurance applies. 6. In the United States, there is no cap on out-of-pocket payments for Medicare beneficiaries.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Figure 3.5. Cost-sharing for outpatient specialist cancer care services including the administration of a medicine in OECD/EU countries

Note: This figure does not take into account potential user charges linked to the use of “reference prices”.

1. Public patients in hospitals only. 2. In Cyprus, people earning less than EUR 135 000 do not share the costs. Beyond this limit, they pay the full cost of care. 3. Public providers only. 4. Public patients in public hospitals only. 5. Cancer care services outside of hospitals. 6. In Switzerland there is a deductible before co-insurance applies. 7. In the United States, there is no cap on out-of-pocket spending for Medicare beneficiaries unless they have supplemental coverage or they have opted for a Medicare Advantage plan. 8. In France, patients may face extra-billing.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Figure 3.6. Cost-sharing for hospital inpatient care for cancer including the administration of a medicine in OECD/EU countries

Note: This figure does not take into account potential user charges linked to the use of “reference prices”.

1. Public patients only. 2. In Cyprus, people earning less than EUR 135 000 do not share the costs. Beyond this limit, they pay the full cost of care. 3. Public hospitals only. 4. Medical Card holders only. 5. Non-Medical Card holders only. 6. France has both co-payment and co-insurance on hospital care, but no co-insurance for hospital services related to cancer care. 7. In Switzerland there is a deductible before co-insurance applies. 8. In the United States, there is no cap on out-of-pocket spending for Medicare beneficiaries unless they have supplemental coverage or they have opted for a Medicare Advantage plan. 9. Private hospitals only.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

136. In the two ESMO studies previously mentioned, the results of a 2014 survey of availability of cancer medicines across 49 European countries and 63 non-European countries were stratified using the level of out-of-pocket spending (“Free”, “<25% cost”, “25-50% cost”, “50-100% cost”, “Full cost (i.e. no coverage)” (Cherny et al., 2016^[61]; Cherny et al., 2017^[62]). The results showed wide disparities across the countries included. In lower-middle- and low-income countries patients had to pay the full costs of about 32% and 58% of anti-cancer medicines included in the WHO Model List of Essential Medicines. In metastatic cancer, including epidermal growth factor receptor (EGFR)-mutated non-small-cell lung cancer, renal cell carcinoma, melanoma, RAS/RAF wild-type metastatic colon cancer, castration-resistant prostate cancer and HER-2 amplified metastatic breast cancer, recently approved medicines for these conditions were only available with large out-of-pocket expenses in less economically developed countries. However, while the study provides a comprehensive analysis on both availability and the “usual” degree of coverage for each medicine, it does not account for the more nuanced elements of co-payment policies, such as the exemption or reduction of co-payments for vulnerable groups, or annual caps on user charges.

137. Various studies have assessed the impact of different cost-sharing mechanisms on access to treatment (Carrera, Kantarjian and Blinder, 2018^[85]; Doshi et al., 2018^[86]; Lentz, Benson and Kircher, 2019^[87]; Lee and Yoon, 2019^[88]). In the United States, for example, higher out-of-pocket costs for Medicare and commercial insurance enrollees have been found to be associated with higher rates of oral anti-cancer prescription abandonment (i.e. prescription not filled) and delayed treatment initiation (Doshi et al., 2018^[86]). A study of the association between high cost-sharing and treatment initiation for metastatic renal cell carcinoma among US Medicare beneficiaries found that those without low-income subsidies were less likely to initiate oral and injected/infused medications than those with these subsidies (26.7% vs. 40.4%) (Li et al., 2018^[89]). In Korea, another study found that catastrophic health spending in households with cancer patients was more frequent among those with National Health Insurance than those receiving Medical Aid benefits⁵³, and more frequent among those with private health insurance compared to those without private insurance (Lee and Yoon, 2019^[88]). In Ireland, a report by the Irish Cancer Society highlighted the financial challenges experienced by 514 cancer patients and their carers who responded to an online survey between May and June 2019 (Irish Cancer Society, 2019^[90]). The challenges included issues such as income and the workplace, the cost of medicines and hospital stays, additional bills at home, and medical card insurance. The average cost per month for medicines was EUR 158 per person.

⁵³ In Korea, national health insurance provides coverage for all citizens, with Medical Aid further supporting lower income groups. See <https://www.hira.or.kr/dummy.do?pgmid=HIRAJ01000006002>, consulted on 18 March 2020.

3.6.2. Medicine prices may affect affordability for patients

138. Cost-sharing design certainly affects the affordability of medicines, but medicine prices also matter, especially when cost-sharing requirements take the form of co-insurance, i.e. a fixed proportion of the price of the medicine⁵⁴. While a co-insurance rate of 10 or 20% may be manageable for a large share of the population taking low-cost medicines, it quickly becomes unaffordable for high cost treatments.

139. The impact of different approaches to pricing on the cost, availability and affordability of cancer medicines was extensively reviewed in the WHO report *Pricing of cancer medicines and its impacts* (World Health Organization, 2018^[2]). The report highlights that many countries have a form of price regulation, with the objective of providing necessary treatment to patients at affordable prices, and to ensure financial sustainability of health systems. Some authorities set prices directly, while others indirectly regulate prices by setting thresholds for public funding. The United States does not utilise price regulation except in a small number of federal programmes, which may in part account for the recent rapid growth in cancer drug prices.

140. Many studies have found that prices of new oncology medicines in the United States are higher than in other countries, even though price differences vary across studies. For all medicines approved by the FDA between 2000 and 2009 for cancer indications, the Australian PBS price was on average 41% lower than the sales price in the United States (Wilson and Cohen, 2011^[91]).⁵⁵ For 29 drugs with cancer indications approved by both the FDA and the EMA between 2000 and 2011, in 2013 the average *list* prices in four European countries (England and Wales, France, Germany, and Netherlands) were 8% lower than the average sales price in the United States, on a per dose or treatment cycle basis (Cohen, Malins and Shahpurwala, 2013^[92]).

141. Other studies have assessed the affordability of medicines by adjusting drug prices for differences in wealth. In a 2017 study, the monthly costs of treatment with individual cancer medicines were adjusted by GDP per capita to compare affordability among seven countries, including the United States and the United Kingdom (Goldstein et al., 2017^[93]). The results showed that *affordability* in middle-income countries (India, China, and South Africa) was poorer than in high-income countries (Australia, Israel, the United States and the United Kingdom), suggesting that prices were only being partly adjusted for capacity to pay. The study was, however, based on list prices and not on actual sales prices, and the metric does not provide information on affordability for individual patients, which may vary within countries.

⁵⁴ In the United States, Medicare beneficiaries who have limited income and resources may get help paying for their Medicare Part A and Part B deductibles, premiums, coinsurance and co-payment costs from Medicaid. Medicaid may also cover additional services beyond those provided under Medicare. Individuals entitled to Medicare and eligible for some form of Medicaid benefit are often referred to as “dual-eligible” beneficiaries. In 2018 there were about 12 million dual-eligibles. See https://www.cms.gov/Medicare-Medicaid-Coordination/Medicare-and-Medicaid-Coordination/Medicare-Medicaid-Coordination-Office/Downloads/MMCO_Factsheet.pdf

⁵⁵ Both studies converted prices into US dollars to compare prices in multiple countries. The pricing data were retrieved from IMS Health and/or national authority websites.

4. Conclusions

142. A variety of strategies have been adopted by countries to address the identified challenges in managing oncology medicines i.e. increasing uncertainty at the time of marketing authorisation; pricing of products with multiple indications of variable cost-effectiveness; pricing of products used in combination regimens; and budget impact driven by increasing volumes and prices. The first section of the report showed that:

- The principal response to uncertainty about clinical benefit at the time of launch is the use of managed entry agreements, some of which are based on the performance of products in “real-life”. However, as shown in a previous OECD report (Wenzl and Chapman, 2019^[24]), payers have mostly sought to mitigate financial risks through the use of these agreements, with less attention given to the generation of additional evidence.
- Several countries do not have the information infrastructure needed to track the use of oncology products by indication. Hence, while some countries adhere to the concept of indication-based pricing (i.e. pricing mechanisms that enable payers to vary the price paid for a drug according to its perceived value in different indications), they can only adjust product prices based on expected utilisation. The problem is naturally the same when price adjustments are needed for products used in combination regimens.
- While both unit and aggregate expenditure on oncology products have steadily increased over time, on average retail pharmaceutical expenditures as a proportion of gross domestic product (GDP) have been stable over the past decade, the result of factors that include the application of budget constraints and spending caps. However substantial growth has been recorded in expenditures on medicines administered to inpatients and in hospital outpatient settings; this is not captured by data on retail expenditure.
- Some countries have established capped, earmarked budgets for innovative oncology medicines (e.g. Italy) or for the temporary coverage of medicines of uncertain cost-effectiveness, pending the generation of further evidence (e.g. England). Their impact on the overall efficiency of pharmaceutical expenditures remains unknown.

143. Policy options for reducing uncertainty concerning the benefits of oncology medicines, and for improving the monitoring of use and associated expenditure include:

- **Strengthening the domestic information landscape through routine tracking of use by indication** – this could inform ex-post price adjustments, support the monitoring of expenditures, and contribute to the gathering of “real world” evidence on the performance of these medicines.
- **Improving the design of performance-based managed entry agreements to support the generation and collection of on-market data** – this would require the collection of utilisation and relevant clinical outcome data for products subject to these agreements. Cross-national harmonisation of outcome metrics, as well as data aggregation and information-sharing across payers and countries is highly desirable, particularly for products targeting small populations.
- **Enhancing international collaboration and information sharing to improve countries’ collective capacity to address clinical and economic uncertainties** - this could include combining efforts to address evidence gaps through, for example, aggregating routinely collected

data at national levels or building multi-country registries. This could also include greater collaboration and engagement between pharmaceutical companies, regulators and health technology assessment (HTA) entities.

144. The second part of this report presents important new information on accessibility and coverage for a sample of oncology medicines across 5 cancer sub-types in 23 countries, as well as new information on time to access for a subset of recent 31 product/indication pairs (comprising products approved in the United States since 2014). The information confirms that access to oncology medicines is unequal across OECD/EU countries.

- Of the 109 product/indication pairs in the sample, the United States had the largest proportion approved and covered (by Medicare), followed by Denmark and Germany (96%, 91%, and 88%, respectively). Chile and Malta had the smallest proportion approved and covered (47% and 46% respectively). Access was more homogeneous across countries for product/indications included in the WHO 21st *Model List of Essential Medicines* (WHO-EML), but, conversely, more heterogeneous for recently approved product/indication pairs, due to the fact that not all of them are yet approved (or launched) in all countries. The number of medicines approved and covered also varied according to cancer type. However, all medicines included in the WHO-EML, and at least one medicine in each pharmacological subgroup, were covered in almost all countries in each cancer type.
- Marketing and coverage decisions for the 31 recent product/indications occurred at different times across OECD/EU countries, with first marketing authorisation granted in the United States in 84% of cases. In individual countries/regions, coverage occurred on average across product/indications 12 to 17 months after their first marketing authorisation in the sample of countries surveyed. For individual product/indications, the time between first marketing authorisation and coverage in a given country ranged from 1 to 66 months (more than 5 years). This reflects both companies' launch sequences, as well as processing times for marketing authorisation, and pricing and coverage decisions.
- At country level, the regulatory review period (including any clock-stops) ranged from 7 months in the United States, to 13 months in the European Economic Area. The time between application and granting of coverage ranged from 4 months in Sweden, to 27 months in Malta. The average total time from application for marketing authorisation to coverage ranged from 9 months in Israel and 11 months in Japan, to 52 months in Malta.

145. Inequities in access were also reported *within* countries. These can be attributed to several factors:

- While most OECD/EU countries make coverage decisions at national level, and which are generally valid across all settings of care, regions or population groups, there are some exceptions (e.g. Canada, some Nordic countries and United States). Beyond this, when sub-national governments have responsibility for inpatient care, variable budget constraints and financing arrangements may lead to differences in access. In some of them, however, efforts are being made to harmonise coverage decisions (e.g. Canada, Norway) or access (e.g. Italy).
- The design of cost-sharing in different care settings can also affect access. In 13 countries, patients can access oncology medicines for self-administration free of charge, or with a fixed co-payment, often adjusted according to ability to pay. In other countries, user charges take the form of co-insurance, with contributions increasing with the price of the medicine. In most countries, inpatient and outpatient cancer care services, including administration of injectable products, are free of charge when delivered by public providers. Almost all countries have a cap on user charges. These caps, where they exist, are defined in absolute or relative terms (e.g. a fixed amount or a proportion of household income); they typically represent less than 1% to 2% of the average wage in European countries but may exceed 9% and 10% of the average wage in the United States and Korea.

respectively. In these two countries, high co-payments have been shown to impair access or lead to catastrophic health spending in households of patients with cancer.

146. Patients and clinicians are increasingly interested in international comparisons of access to medicines, and these can provide useful benchmarks for policy makers. However, **access needs to be understood within the context of each country's health care system** and the information collected on access in this study has several limitations. First, in most cases, it does not take into account early access schemes, which provide access to promising medicines for high unmet medical needs prior to marketing authorisation or coverage decision. Moreover, individual drug availability and coverage data do not provide a complete picture of access to appropriate treatments for patients in need. Hofmarcher et al. (2019^[4]) showed in a recent report on EU countries that consumption levels, even for covered medicines, vary widely across countries, probably beyond what could reasonably be explained by differences in burden of disease and clinical practice guidelines. They noted that consumption in Eastern European countries was well below that of wealthier European countries. This suggests that, beyond availability and coverage, access is likely to be impaired by funding arrangements, and potentially by the increasing prevalence of supply interruptions and stock shortages.

147. As noted above, tracking the utilisation of oncology medicines by indication can inform assessments of uptake, and highlight differences in access across regions and/or coverage programmes that can reflect challenges in individual affordability. To support affordable access, countries could consider **minimising (or even eliminating) patient contributions, and applying fixed co-payments rather than co-insurance**, with safety nets to preserve affordability and avoid catastrophic costs for patients and households.

148. All contributing countries recognised that managing and sustaining equitable access to oncology medicines is an ongoing challenge for which there are no simple solutions. Considerable value was seen in **improving the quality of clinical and economic evidence, and enhancing international cooperation and information sharing** as much as possible. This could include, for example, pursuing greater international harmonisation of regulatory requirements for clinical trials, or developing a framework for international public funding of comparative clinical trials to enhance evidence for HTA.

149. Finally, there is a myriad of related issues (and potential policy options) that fall within the rubric of challenges in access to oncology medicines, but lie beyond the scope of this working paper. Some of these issues also pertain to providing and sustaining access to novel and expensive medicines used in other therapeutic domains, and for which a range of policy options were identified in the recent OECD Report *Pharmaceutical Innovation and Access to Medicines* (OECD, 2018^[72]).

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Annexe A. OECD data collection

The content of this paper is based on information available from public sources, including the peer-reviewed literature, grey literature and documents published by payers and government agencies, survey data, and experience from stakeholders collected by the OECD Secretariat during a two-day workshop on oncology medicines.

Expert interviews and survey

The key challenges identified in managing and accessing oncology medicines were elicited from a series of preliminary discussions with experts from a sample of OECD member countries (France, Canada, Poland and the Netherlands).

In September 2019, the OECD Secretariat sent a survey to a total of 41 countries, including OECD member countries and EU Member States comprising

1. a MS-word document with questions on challenges encountered in access to oncology medicines and policies and approaches adopted to address them;
2. a MS-word document with prefilled information on cost-sharing requirements for oncology medicines and other health care services for review, update, and amendment; and
3. a MS-excel tabular spreadsheet with information to complete on several aspects of access concerning a sample of oncology medicines used in five cancer types.

A total of 25 countries responded to at least one part of the survey Table A A.1.

Table A A.1. Responses to OECD survey

Country	1. Policy questionnaire	2. Cost-sharing	3. Access survey
Australia	yes	no ¹	yes
Belgium	yes	yes	yes
Canada	yes	yes	no
Chile	yes	no	yes
Cyprus	yes	yes	yes
Czech Republic	no	yes	yes
Denmark	yes	yes	yes
Estonia	yes	yes	yes
France	yes	yes	yes
Germany	yes	yes	yes
Greece	yes	yes	yes
Hungary	yes	yes	yes
Ireland	yes	yes	yes
Israel	yes	yes	yes
Italy	yes	yes	no
Japan	yes	yes	yes
Korea	yes	yes	yes
Latvia	yes	yes	yes
Lithuania	yes	yes	yes
Malta	yes	yes	yes
Norway	yes	yes	yes
Sweden	yes	yes	yes

Country	1. Policy questionnaire	2. Cost-sharing	3. Access survey
Switzerland	yes	yes	yes
United Kingdom (England only)	yes	no ¹	yes
United States	yes	yes	yes
Count of countries	24	22	23

Note:

1. Information on cost-sharing requirements was updated by the Secretariat using publicly available sources.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Part 1, a policy questionnaire on key challenges in managing oncology medicines, contained 30 questions drawing on themes arising from a literature review and a series of preliminary discussions with experts from selected OECD member countries (France, Canada, Poland and the Netherlands).

Part 2, a pre-filled document with information on cost-sharing was sent to countries for completion and/ or revision. Initial information was based on information collected by the OECD as part of the *Health Systems Characteristics Survey* in 2012 and updated for the working paper on *Health Care Coverage in OECD Countries* in 2012, published in 2016 (Paris et al., 2016^[94]). Countries were asked to provide information related to covered oncology medicines, and to inpatient and specialist services that included the administration of covered oncology medicines.

Part 3 drew on information presented in the recent WHO Report *Pricing of Cancer Medicines and its Impacts* (World Health Organization, 2018^[2]), which was in turn based on the results of two ESMO surveys (Cherny et al., 2016^[61]; Cherny et al., 2017^[62]). A subset of the medicines was selected based on cancers with significant prevalence in OECD countries, with the addition of all oncology medicines subsequently approved in the United States or Europe as of July 2019, as well as those included in the 21st WHO *Model List of Essential Medicines* (WHO-EML) (2019^[63]). The intention was to capture those indications for which there are a large number of new medicines available, including immunotherapies. The list was refined in order to create a manageable sample, with no value judgements regarding the final indications and medicines chosen. This analysis could be extended in the future.

The final sample comprised 101 oncology product/indication pairs and 8 ancillary products (for supportive care) used in the following indications: metastatic breast cancer, non-small cell lung cancer, colorectal cancer, melanoma, and multiple myeloma (see Table A A.2). Medicines were classified by the WHO Collaborating Centre for Drug Statistics Methodology (WHOC) Anatomical Therapeutic Chemical (ATC) code (2019^[65]). The following information was sought for the 109 product/indication pairs in the sample: regulatory approval and coverage status; setting of administration; generic / biosimilar protection or number of generic/biosimilar products available. In order to assess access to novel products, further information was sought for the 31 product/indication pairs approved in the United States since 2014. This included the date of application for marketing authorisation; date of marketing authorisation; date of application for coverage determination; date of coverage determination; and any applicable coverage restrictions. The Secretariat added dates for marketing authorisation for those countries with central authorisation by the European Commission.

Inconsistencies in initial survey responses were clarified with relevant experts.

Table A A.2. Final product/indication sample for OECD access survey

109 product/indication pairs included in the final sample, across five cancer types and supportive care

Indication	Active substance	ATC Code	ATC-4 Level	WHO-EML	Vintage ¹
Metastatic breast cancer	abemaciclib	L01XE50	protein kinase inhibitors	no	new
Metastatic breast cancer	anastrozole	L02BG03	aromatase inhibitors	yes	old
Metastatic breast cancer	bevacizumab	L01XC07	monoclonal antibodies	no	old
Metastatic breast cancer	capecitabine	L01BC06	pyrimidine analogues	yes	old
Metastatic breast cancer	carboplatin	L01XA02	platinum compounds	no	old
Metastatic breast cancer	cisplatin	L01XA01	platinum compounds	no	old
Metastatic breast cancer	cyclophosphamide	L01AA01	nitrogen mustard analogues	yes	old
Metastatic breast cancer	docetaxel	L01CD02	taxanes	yes	old
Metastatic breast cancer	doxorubicin - liposomal	L01DB01	anthracyclines and related substances	no	old
Metastatic breast cancer	doxorubicin	L01DB01	anthracyclines and related substances	yes	old
Metastatic breast cancer	eribulin	L01XX41	other antineoplastic agents	no	old
Metastatic breast cancer	everolimus	L01XE10	protein kinase inhibitors	no	old
Metastatic breast cancer	exemestane	L02BG06	aromatase inhibitors	no	old
Metastatic breast cancer	fluorouracil	L01BC02	pyrimidine analogues	no	old
Metastatic breast cancer	fulvestrant	L02BA03	anti-oestrogens	no	old
Metastatic breast cancer	ixabepilone	L01DC04	other cytotoxic antibiotics	no	old
Metastatic breast cancer	lapatinib	L01XE07	protein kinase inhibitors	no	old
Metastatic breast cancer	letrozole	L02BG04	aromatase inhibitors	no	old
Metastatic breast cancer	olaparib	L01XX46	other antineoplastic agents	no	new
Metastatic breast cancer	paclitaxel	L01CD01	taxanes	yes	old
Metastatic breast cancer	palbociclib	L01XE33	protein kinase inhibitors	no	new
Metastatic breast cancer	pertuzumab	L01XC13	monoclonal antibodies	no	old
Metastatic breast cancer	ribociclib	L01XE42	protein kinase inhibitors	no	new
Metastatic breast cancer	talazoparib	L01XX60	other antineoplastic agents	no	new
Metastatic breast cancer	tamoxifen	L02BA01	anti-oestrogens	yes	old
Metastatic breast cancer	toremifene	L02BA02	anti-oestrogens	no	old
Metastatic breast cancer	trastuzumab emtansine	L01XC14	monoclonal antibodies	no	old
Metastatic breast cancer	trastuzumab	L01XC03	monoclonal antibodies	yes	old
Metastatic breast cancer	vinorelbine	L01CA04	vinca alkaloids and analogues	yes	old
Non-small cell lung cancer	afatinib	L01XE13	protein kinase inhibitors	no	old
Non-small cell lung cancer	alectinib	L01XE36	protein kinase inhibitors	no	new
Non-small cell lung cancer	atezolizumab	L01XC32	monoclonal antibodies	no	new
Non-small cell lung cancer	bevacizumab	L01XC07	monoclonal antibodies	no	old
Non-small cell lung cancer	brigatinib	L01XE43	protein kinase inhibitors	no	new
Non-small cell lung cancer	carboplatin	L01XA02	platinum compounds	yes	old
Non-small cell lung cancer	ceritinib	L01XE28	protein kinase inhibitors	no	new
Non-small cell lung cancer	cisplatin	L01XA01	platinum compounds	yes	old
Non-small cell lung cancer	crizotinib	L01XE16	protein kinase inhibitors	no	old
Non-small cell lung cancer	dabrafenib	L01XE23	protein kinase inhibitors	no	old
Non-small cell lung cancer	dacomitinib	L01XE47	protein kinase inhibitors	no	new
Non-small cell lung cancer	docetaxel	L01CD02	taxanes	no	old
Non-small cell lung cancer	doxorubicin	L01DB01	anthracyclines and related substances	no	old
Non-small cell lung cancer	durvalumab	L01XC28	monoclonal antibodies	no	new
Non-small cell lung cancer	erlotinib	L01XE03	protein kinase inhibitors	yes	old
Non-small cell lung cancer	etoposide	L01CB01	podophyllotoxin derivatives	yes	old
Non-small cell lung cancer	gefitinib	L01XE02	protein kinase inhibitors	no	old
Non-small cell lung cancer	gemcitabine	L01BC05	pyrimidine analogues	yes	old
Non-small cell lung cancer	lorlatinib	L01XE44	protein kinase inhibitors	no	new
Non-small cell lung cancer	necitumumab	L01XC22	monoclonal antibodies	no	new
Non-small cell lung cancer	nivolumab	L01XC17	monoclonal antibodies	no	new

Indication	Active substance	ATC Code	ATC-4 Level	WHO-EML	Vintage ¹
Non-small cell lung cancer	osimertinib	L01XE35	protein kinase inhibitors	no	new
Non-small cell lung cancer	paclitaxel	L01CD01	taxanes	yes	old
Non-small cell lung cancer	pembrolizumab	L01XC18	monoclonal antibodies	no	new
Non-small cell lung cancer	pemetrexed	L01BA04	folic acid analogues	no	old
Non-small cell lung cancer	ramucirumab	L01XC21	monoclonal antibodies	no	new
Non-small cell lung cancer	trametinib	L01XE25	protein kinase inhibitors	no	old
Non-small cell lung cancer	vinorelbine	L01CA04	vinca alkaloids and analogues	yes	old
Colorectal cancer	afibercept	L01XX44	other antineoplastic agents	no	old
Colorectal cancer	bevacizumab	L01XC07	monoclonal antibodies	no	old
Colorectal cancer	capecitabine	L01BC06	pyrimidine analogues	yes	old
Colorectal cancer	cetuximab	L01XC06	monoclonal antibodies	no	old
Colorectal cancer	fluorouracil	L01BC02	pyrimidine analogues	yes	old
Colorectal cancer	irinotecan	L01XX19	other antineoplastic agents	yes	old
Colorectal cancer	mitomycin C	L01DC03	other cytotoxic antibiotics	no	old
Colorectal cancer	nivolumab	L01XC17	monoclonal antibodies	no	new
Colorectal cancer	oxaliplatin	L01XA03	platinum compounds	yes	old
Colorectal cancer	panitumumab	L01XC08	monoclonal antibodies	no	old
Colorectal cancer	pembrolizumab	L01XC18	monoclonal antibodies	no	new
Colorectal cancer	raltitrexed	L01BA03	folic acid analogues	no	old
Colorectal cancer	ramucirumab	L01XC21	monoclonal antibodies	no	new
Colorectal cancer	regorafenib	L01XE21	protein kinase inhibitors	no	old
Colorectal cancer	trifluridine / tipiracil	L01BC59	pyrimidine analogues	no	new
Melanoma	high-dose IL-2 - aldesleukin	L03AC01	interleukins	no	old
Melanoma	binimetinib	L01XE41	protein kinase inhibitors	no	new
Melanoma	cobimetinib	L01XE38	protein kinase inhibitors	no	new
Melanoma	dabrafenib	L01XE23	protein kinase inhibitors	no	old
Melanoma	dacarbazine	L01AX04	other alkylating agents	no	old
Melanoma	encorafenib	L01XE46	protein kinase inhibitors	no	new
Melanoma	fotemustine	L01AD05	nitrosoureas	no	old
Melanoma	interferon	L03AB	interferons	no	old
Melanoma	ipilimumab	L01XC11	monoclonal antibodies	no	old
Melanoma	nivolumab	L01XC17	monoclonal antibodies	yes	new
Melanoma	pembrolizumab	L01XC18	monoclonal antibodies	yes	new
Melanoma	talimogene laherparepvec	L01XX51	other antineoplastic agents	no	new
Melanoma	temozolomide	L01AX03	other alkylating agents	no	old
Melanoma	trametinib	L01XE25	protein kinase inhibitors	no	old
Melanoma	vemurafenib	L01XE15	protein kinase inhibitors	no	old
Multiple myeloma	bortezomib	L01XX32	other antineoplastic agents	yes	old
Multiple myeloma	carfilzomib	L01XX45	other antineoplastic agents	no	old
Multiple myeloma	cyclophosphamide	L01AA01	nitrogen mustard analogues	yes	old
Multiple myeloma	daratumumab	L01XC24	monoclonal antibodies	no	new
Multiple myeloma	doxorubicin	L01DB01	anthracyclines and related substances	yes	old
Multiple myeloma	elotuzumab	L01XC23	monoclonal antibodies	no	new
Multiple myeloma	interferon alfa-2b	L03AB	interferons	no	old
Multiple myeloma	ixazomib	L01XX50	other antineoplastic agents	no	new
Multiple myeloma	lenalidomide	L04AX04	other immunosuppressants	yes	old
Multiple myeloma	melfalan	L01AA03	nitrogen mustard analogues	yes	old
Multiple myeloma	panobinostat	L01XX42	other antineoplastic agents	no	new
Multiple myeloma	plerixafor	L03AX16	other immunostimulants	no	old
Multiple myeloma	pomalidomide	L04AX06	other immunosuppressants	no	old
Multiple myeloma	thalidomide	L04AX02	other immunosuppressants	yes	old
Ancillary treatment	calcium folinate - leucovorin	V03AF03	detoxifying agents	yes	old
Ancillary treatment	dexamethasone	H02AB02	corticosteroids	yes	old
Ancillary treatment	epoetin alfa	B03XA01	other anti-anaemic preparations	no	old

Indication	Active substance	ATC Code	ATC-4 Level	WHO-EML	Vintage ¹
Ancillary treatment	epoetin zeta	B03XA02	other anti-anaemic preparations	no	old
Ancillary treatment	filgrastim	L03AA02	colony stimulating factors	yes	old
Ancillary treatment	lipegfilgrastim	L03AA14	colony stimulating factors	no	old
Ancillary treatment	pegfilgrastim	L03AA13	colony stimulating factors	no	old
Ancillary treatment	prednisolone	H02AB06	corticosteroids	yes	old

Note: ATC Anatomical Therapeutic Chemical, WHO-EML World Health Organization's 21st Model List of Essential Medicines
Product/indication pairs were classified by ATC-4 code and level (2019_[65]), according to whether they were included in the WHO-EML (2019_[63]), and whether they had entered the United States market since 2014.

1. New refers to product/indication pairs approved in the United States since 2014.

Source: Authors, based on 2019 OECD survey on challenges in access to oncology medicines.

Workshop

The OECD/EU Workshop on Oncology Medicines took place on 2-3 December 2019 at the European Commission, Brussels. Twenty-two experts from 17 EU Member States attended the meeting; as well as representatives of European Commission DG Santé, WHO, invited experts from regulatory and HTA agencies and the OECD Secretariat. Experts from Member States were invited to provide feedback and advice around the current OECD project on Challenges in Access to Oncology Medicines and share their experience. The last session on Day 2 was opened to stakeholders; six representatives from European Federation of Pharmaceutical Industries and Associations (EFPIA), two from Medicines for Europe (MfE), and two from European Cancer Leagues (ECL - patient association) attended to share their perspectives on the oncology topic. The primary focus of this workshop was to discuss preliminary results of the OECD oncology survey.

Annexe B. OECD access survey – limitations and country-specific caveats

Table A B.1 below outlines limitations to the data, or assumptions made by the 23 countries who responded to Part 3 of the OECD survey on access to the sample of 109 product/indication pairs. The table also indicates the dates of survey submission by respondents (ranging from 20 September 2019 for Cyprus to 15 January 2020 for Chile), which is important since the evolution in approvals and coverage decisions in oncology is rapid. A medicine indicated as “not approved” or “not covered” in a country may be a medicine which is not yet approved or covered or for which an application for marketing authorisation or (more likely) coverage led to a negative outcome. This table should be read in conjunction with Table 3.4 on level of coverage decisions.

Table A B.1. Country-specific caveats

Country	Submission date	Notes
Australia	08/12/19	<ul style="list-style-type: none"> - Information was only provided for selected product/indication pairs - Information provided only covers the Pharmaceutical Benefits Scheme, which provides national-level coverage for medicines supplied in settings other than to public hospital inpatients. Coverage of medicines administered during to public hospital inpatients of public hospitals may vary across States and territories.
Belgium	08/10/19 (amended 09/03/20)	<ul style="list-style-type: none"> - For products that are “approved and covered”, the originator may no longer be reimbursed or available, or the product may only be covered under certain conditions. - Coverage was granted for two product/indication pairs after 20/09/19 (the date of the first respondent submission) - National-level coverage decision
Chile	15/01/20	<ul style="list-style-type: none"> - Marketing authorisation was granted for one product/indication pair after 20/09/19 (the date of the first respondent submission)
Cyprus	20/09/19	<ul style="list-style-type: none"> - Application for coverage can be made by pharmaceutical companies and doctors prior to EU marketing authorisation date (e.g. based on FDA approval). Once a medicine is approved by EMA, it is available for patients to access without any coverage scheme; in many cases, the government covers the cost of these medicines. - Some medicines with an EU marketing authorisation may be listed as “not approved” as they have not been launched on the market in Cyprus. - National-level coverage decision
Czech Republic	27/11/19	<ul style="list-style-type: none"> - Two products listed as “not approved” as relevant indication not in Summary of Product Characteristics (products are listed for use in these indications in national guidelines) - National-level coverage decision
Denmark	07/11/19 (amended 09/03/20)	<ul style="list-style-type: none"> - National-level coverage decision
Estonia	23/09/19	<ul style="list-style-type: none"> - Coverage was granted for two product/indication pairs after 20/09/19 (the date of the first respondent submission) - National-level coverage decision
France	18/11/19 (amended 06/03/20)	<ul style="list-style-type: none"> - National-level coverage decision and coverage - Delays in coverage may be due to price negotiation
Germany	25/11/19 (amended 27/02/20)	<ul style="list-style-type: none"> - National-level coverage decision and coverage
Greece	30/09/19	<ul style="list-style-type: none"> - For new oncology medicines authorised through the EMA centralised procedure, the answer “not approved” implies that the new medicines has not yet been launched in Greece, either because the company has not yet applied for a price, or because the pricing procedure is still in progress. - The answer “approved but not covered” may mean that the product does not yet have a price, the product is

Country	Submission date	Notes
Greece (cont.)		approved through a type of early patient access scheme, the product has a price but has not yet been included in the positive list, or the product could be reimbursed in limited cases as an imported medicine or for off-label use etc - National-level coverage decision
Hungary	28/10/19	- Medicines may have restricted and/or conditional availability in a named -patient programme - It is not possible for the marketing authorisation holder to apply for coverage prior to the date of marketing authorisation of the product - National-level coverage decision
Ireland	19/11/19 (amended 03/12/19)	- The answer "approved but not covered" may mean that the company has not yet applied for coverage or that the application is being processed. - Coverage was granted for two product/indication pairs after 20/09/19 (the date of the first respondent submission) - National-level coverage decisions for high-cost medicines administered in outpatient and inpatient care settings
Israel	12/01/20	- National-level coverage decisions are made once a year (during October-December), with decisions put into effect in January of the following year - Date of marketing authorisation reflects the final approval date for a pharmaceutical. It may have received a positive opinion from the Advisory Committee prior to this date, at which point it may be included in the National List of Health Services. Thus the date of marketing authorisation may be after the date of coverage decision.
Japan	14/10/19	- Reimbursement of a new pharmaceutical is listed within 60 days (within 90 days at the latest) from the time of approval. The reimbursement process starts immediately after approval of the medicine, with an additional indication being covered by public health insurance from the day of approval of the medicine. Prices are not negotiated; reimbursement prices are set by the government's official pricing formula. - National-level coverage decisions
Korea	21/10/19	- National-level coverage decisions
Latvia	21/10/19 (amended 11/03/20)	- The answer "not approved" may mean that the product has not been launched in Latvia - In 2018, only ~23% (608) of 2637 names of products authorised through the centralised procedure at EU level were launched in Latvia. On the one hand some marketing authorisation holders are not interested in launching their products in Latvia (small market, low purchasing power etc.). On the other hand, affordability is the cornerstone of access. Usually the medicines are available to patients only if the costs are covered by the state i.e. if the medicine is included in the Positive List (i.e. the medicine is cost-effective and the state can afford it). In order to decide whether to include the medicine in the Positive list, the cost-effectiveness and budget impact of the medicine need to be evaluated by the competent authorities. If the medicine is not cost-effective at the offered price or there is insufficient budget for reimbursement the medicine does not receive coverage. - National-level coverage decision
Lithuania	15/10/19 (amended 05/11/19)	- National-level coverage decision
Malta	08/10/19 (amended 09/03/20)	- The answer "approved but not covered" may mean that the product was approved but is in the process of being procured through tender - National-level coverage decision
Norway	17/10/19 (amended 06/03/20)	- National-level coverage decision, regional financing - For hospital drugs (all oncology treatments), the four regions are responsible for access to medicines for patients. The four regions participate in a Decision Forum. The regions have formally delegated their decision authority to the Decision Forum. The Decision Forum must reach a common decision for all regions that is a national decision. - To complete the survey for the new novel medicines, the web page nyemetoder.no in addition to in house registries were used. For the older medicines, information from the tender was used to complete the survey; information about whether these drugs actually are used for the specific cancer types or not was not available for these drugs. - If the company can provide a dossier at an early stage, application for coverage is possible prior to marketing authorisation - The answer "not approved" may mean that the drug has not been marketed in Norway. - The answer "approved but not covered" may mean that it was not covered at the time of survey completion, awaiting documentation from the company, ongoing assessments or awaiting decisions. - The answer "approved and covered" mainly means covered by hospitals. However in some special cases it may mean that it is covered by primary care sector, in combination with one thing but not another, or a subgroup may be covered but not all groups (e.g. line of therapy, biomarker etc), or temporary coverage has

Country	Submission date	Notes
Norway (cont.)		<p>been applied.</p> <ul style="list-style-type: none"> - Coverage was granted for six product/indication pairs after 20/09/19 (the date of the first respondent submission)
Sweden	14/10/19 (amended 18/12/19)	<ul style="list-style-type: none"> - Information includes both national and, where possible, regional-level coverage decisions. Information for regions was found online and from sales data. - Product-based national-level coverage decisions for outpatient medicines by TLV; all approved indications are subsidised. - Coverage for inpatient medicines is decided by regions, sometimes as soon as it is approved. The regions in Sweden have a process called managed introduction with the New Therapies Council to make sure equal access to medicines to all patients, which is used for some medicines, but not for all. For some medicines, the regions' New Therapies Council asks TLV for an evaluation and makes a recommendation based on that. In some cases, the date of such a relevant recommendation has been used as date of coverage decision.
Switzerland	04/10/19 (amended 19/11/19)	<ul style="list-style-type: none"> - National-level coverage decision and insurer provider network
United Kingdom (England only)	18/10/19 (amended 29/11/19)	<ul style="list-style-type: none"> - The answer "approved and covered" may also mean that the product/indication pair has a patient access scheme or is in the Cancer Drugs Fund with a managed access agreement - National-level coverage decision
United States	20/12/19	<ul style="list-style-type: none"> - The data presented are for Medicare; anti-neoplastics are a protected class under Medicare Part D. - The US has a complex system based around individual health coverage schemes

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Annexe C. OECD access survey – indication-specific results

Table A C.1 to Table A C.6 below present a snapshot summary of regulatory approval and coverage status of the 109 sample product/indication pairs by indication for the 23 countries who responded to this part of the OECD survey. Information is reported as per the country survey submission date (see Table A B.1). Below is a note on how to read information presented in the tables:

- Colour code:

	Not approved (no marketing authorisation for this indication) or not (yet) launched
	Approved but not covered
	Approved and covered
	No information provided

- * = product/indication pair included in the World Health Organization's 21st *Model List of Essential Medicines* (WHO-EML) (2019^[63]).
- † = product/indication pair has been approved since 2014 in the United States.
- ‡ = European Medicines Agency (EMA) marketing authorisation withdrawn.
- § = There is no central marketing authorisation at EU level for this product/indication pair.
- Note for EU members states (and Norway)
 - When a medicine appears as “approved” in one country and “not approved” in another country, it might mean either 1) that the product has been approved before 1995 through national procedures (before systematic centralised marketing authorisation of all oncology medicines); or 2) that the product, although authorised for marketing in all EU countries, has not (yet) been launched on the market in that country for that indication

Table A C.1. Regulatory approval and coverage status of medicines for *metastatic breast cancer*

Active substance	ATC Code	ATC-4 Level	AUS	BEL	CHE	CHL	CYP	CZE	DEU	DNK	EST	FRA	GBR	GRC	HUN	IRL	ISR	JPN	KOR	LTU	LVA	MLT	NOR	SWE	USA
doxorubicin -liposomal	L01DB01	anthracyclines and related substances																							
doxorubicin*	L01DB01	anthracyclines and related substances																							
fulvestrant	L02BA03	anti-estrogens																							
tamoxifen*	L02BA01	anti-estrogens																							
toremifene	L02BA02	anti-estrogens																							
anastrozole*	L02BG03	aromatase inhibitors																							
exemestane	L02BG06	aromatase inhibitors																							
letrozole	L02BG04	aromatase inhibitors																							
bevacizumab	L01XC07	monoclonal antibodies																							
pertuzumab	L01XC13	monoclonal antibodies																							
trastuzumab emtansine	L01XC14	monoclonal antibodies																							
trastuzumab*	L01XC03	monoclonal antibodies																							
cyclophosphamide*	L01AA01	nitrogen mustard analogues																							
carboplatin	L01XA02	platinum compounds																							
cisplatin	L01XA01	platinum compounds																							
abemaciclib†	L01XE50	protein kinase inhibitors																							
everolimus	L01XE10	protein kinase inhibitors																							
lapatinib	L01XE07	protein kinase inhibitors																							
palbociclib†	L01XE33	protein kinase inhibitors																							
ribociclib†	L01XE42	protein kinase inhibitors																							
capecitabine*	L01BC06	pyrimidine analogues																							
fluorouracil	L01BC02	pyrimidine analogues																							
docetaxel*	L01CD02	taxanes																							
paclitaxel*	L01CD01	taxanes																							
vinorelbine*	L01CA04	vinca alkaloids and analogues																							
eribulin	L01XX41	other antineoplastic agents																							
olaparib†	L01XX46	other antineoplastic agents																							
talazoparib†	L01XX60	other antineoplastic agents																							
ixabepilone	L01DC04	other cytotoxic antibiotics																							

Note: Dark blue = not approved i.e. no marketing authorisation for this indication or not (yet) launched; medium blue = approved but not covered; light blue = approved and covered; white = no data provided. * product/indication pair included in the WHO-EML (2019^[63]); † product/indication pair has been approved in the United States since 2014; ‡ EMA marketing authorisation withdrawn. For EU members states (and Norway), when a medicine appears as “approved” in one country and “not approved” in another country, it might mean either 1) that the product has been approved before 1995 through national procedures (before systematic centralised marketing authorisation of all oncology medicines); or 2) that the product, although authorised for marketing in all EU countries, has not (yet) been launched on the market in that country for that indication. Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Table A C.2. Regulatory approval and coverage status of medicines for *non-small cell lung cancer*

Active substance	ATC Code	ATC-4 Level	AUS	BEL	CHE	CHL	CYP	CZE	DEU	DNK	EST	FRA	GBR	GRC	HUN	IRL	ISR	JPN	KOR	LTU	LVA	MLT	NOR	SWE	USA
doxorubicin	L01DB01	anthracyclines and related substances																							
pemetrexed	L01BA04	folic acid analogues																							
atezolizumab†	L01XC32	monoclonal antibodies																							
bevacizumab	L01XC07	monoclonal antibodies																							
durvalumab†	L01XC28	monoclonal antibodies																							
necitumumab†	L01XC22	monoclonal antibodies																							
nivolumab†	L01XC17	monoclonal antibodies																							
pembrolizumab†	L01XC18	monoclonal antibodies																							
ramucirumab†	L01XC21	monoclonal antibodies																							
carboplatin*	L01XA02	platinum compounds																							
cisplatin*	L01XA01	platinum compounds																							
etoposide*	L01CB01	podophyllotoxin derivatives																							
afatinib	L01XE13	protein kinase inhibitors																							
alectinib†	L01XE36	protein kinase inhibitors																							
brigatinib†	L01XE43	protein kinase inhibitors																							
ceritinib†	L01XE28	protein kinase inhibitors																							
crizotinib	L01XE16	protein kinase inhibitors																							
dabrafenib	L01XE23	protein kinase inhibitors																							
dacomitinib†	L01XE47	protein kinase inhibitors																							
erlotinib*	L01XE03	protein kinase inhibitors																							
gefitinib	L01XE02	protein kinase inhibitors																							
lorlatinib†	L01XE44	protein kinase inhibitors																							
osimertinib†	L01XE35	protein kinase inhibitors																							
trametinib	L01XE25	protein kinase inhibitors																							
gemcitabine*	L01BC05	pyrimidine analogues																							
docetaxel	L01CD02	taxanes																							
paclitaxel*	L01CD01	taxanes																							
vinorelbine*	L01CA04	vinca alkaloids and analogues																							

Note: Dark blue = not approved i.e. no marketing authorisation for this indication or not (yet) launched; medium blue = approved but not covered; light blue = approved and covered; white = no data provided. * product/indication pair included in the WHO-EML (2019_[53]); † product/indication pair has been approved in the United States since 2014. For EU members states (and Norway), when a medicine appears as “approved” in one country and “not approved” in another country, it might mean either 1) that the product has been approved before 1995 through national procedures (before systematic centralised marketing authorisation of all oncology medicines); or 2) that the product, although authorised for marketing in all EU countries, has not (yet) been launched on the market in that country for that indication. Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Table A C.3. Regulatory approval and coverage status of medicines for colorectal cancer

Active substance	ATC Code	ATC-4 Level	AUS	BEL	CHE	CHL	CYP	CZE	DEU	DNK	EST	FRA	GBR	GRC	HUN	IRL	ISR	JPN	KOR	LTU	LVA	MLT	NOR	SWE	USA
raltitrexed	L01BA03	folic acid analogues																							
bevacizumab	L01XC07	monoclonal antibodies																							
cetuximab	L01XC06	monoclonal antibodies																							
nivolumab†§	L01XC17	monoclonal antibodies																							
panitumumab	L01XC08	monoclonal antibodies																							
pembrolizumab†§	L01XC18	monoclonal antibodies																							
ramucirumab†	L01XC21	monoclonal antibodies																							
oxaliplatin*	L01XA03	platinum compounds																							
regorafenib	L01XE21	protein kinase inhibitors																							
capecitabine*	L01BC06	pyrimidine analogues																							
fluorouracil*	L01BC02	pyrimidine analogues																							
trifluridine / tipiracil†	L01BC59	pyrimidine analogues																							
afibercept	L01XX44	other antineoplastic agents																							
irinotecan*	L01XX19	other antineoplastic agents																							
mitomycin C	L01DC03	other cytotoxic antibiotics																							

Note: Dark blue = not approved i.e. no marketing authorisation for this indication or not (yet) launched; medium blue = approved but not covered; light blue = approved and covered; white = no data provided.

* product/indication pair included in the WHO-EML (2019_[63]); † product/indication pair has been approved in the United States since 2014; § There is no central marketing authorisation at EU level for this product/indication pair.

For EU members states (and Norway), when a medicine appears as “approved” in one country and “not approved” in another country, it might mean either 1) that the product has been approved before 1995 through national procedures (before systematic centralised marketing authorisation of all oncology medicines); or 2) that the product, although authorised for marketing in all EU countries, has not (yet) been launched on the market in that country for that indication.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Table A C.4. Regulatory approval and coverage status of medicines for *melanoma*

Active substance	ATC Code	ATC-4 Level	AUS	BEL	CHE	CHL	CYP	CZE	DEU	DNK	EST	FRA	GBR	GRC	HUN	IRL	ISR	JPN	KOR	LTU	LVA	MLT	NOR	SWE	USA
interferon	L03AB	interferons																							
high-dose il-2 - aldesleukin	L03AC01	interleukins																							
ipilimumab	L01XC11	monoclonal antibodies																							
nivolumab*†	L01XC17	monoclonal antibodies																							
pembrolizumab*†	L01XC18	monoclonal antibodies																							
fotemustine	L01AD05	nitrosoureas																							
binimetinib†	L01XE41	protein kinase inhibitors																							
cobimetinib†	L01XE38	protein kinase inhibitors																							
dabrafenib	L01XE23	protein kinase inhibitors																							
encorafenib†	L01XE46	protein kinase inhibitors																							
trametinib	L01XE25	protein kinase inhibitors																							
vemurafenib	L01XE15	protein kinase inhibitors																							
dacarbazine	L01AX04	other alkylating agents																							
temozolomide	L01AX03	other alkylating agents																							
talimogene laherparepvec†	L01XX51	other antineoplastic agents																							

Note: Dark blue = not approved i.e. no marketing authorisation for this indication or not (yet) launched; medium blue = approved but not covered; light blue = approved and covered; white = no data provided.

* product/indication pair included in the WHO-EML (2019_[63]); † product/indication pair has been approved in the United States since 2014.

For EU members states (and Norway), when a medicine appears as “approved” in one country and “not approved” in another country, it might mean either 1) that the product has been approved before 1995 through national procedures (before systematic centralised marketing authorisation of all oncology medicines); or 2) that the product, although authorised for marketing in all EU countries, has not (yet) been launched on the market in that country for that indication.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Table A C.5. Regulatory approval and coverage status of medicines for *multiple myeloma*

Active substance	ATC Code	ATC-4 Level	AUS	BEL	CHE	CHL	CYP	CZE	DEU	DNK	EST	FRA	GBR	GRC	HUN	IRL	ISR	JPN	KOR	LTU	LVA	MLT	NOR	SWE	USA
doxorubicin*	L01DB01	anthracyclines and related substances																							
interferon alfa-2b	L03AB	interferons																							
daratumumab†	L01XC24	monoclonal antibodies																							
elotuzumab†	L01XC23	monoclonal antibodies																							
cyclophosphamide*	L01AA01	nitrogen mustard analogues																							
melphalan*	L01AA03	nitrogen mustard analogues																							
bortezomib*	L01XX32	other antineoplastic agents																							
carfilzomib	L01XX45	other antineoplastic agents																							
ixazomib†	L01XX50	other antineoplastic agents																							
panobinostat†	L01XX42	other antineoplastic agents																							
plerixafor	L03AX16	other immunostimulants																							
lenalidomide*	L04AX04	other immunosuppressants																							
pomalidomide	L04AX06	other immunosuppressants																							
thalidomide*	L04AX02	other immunosuppressants																							

Note: Dark blue = not approved i.e. no marketing authorisation for this indication or not (yet) launched; medium blue = approved but not covered; light blue = approved and covered; white = no data provided.

* product/indication pair included in the WHO-EML (2019_[63]); † product/indication pair has been approved in the United States since 2014.

For EU members states (and Norway), when a medicine appears as “approved” in one country and “not approved” in another country, it might mean either 1) that the product has been approved before 1995 through national procedures (before systematic centralised marketing authorisation of all oncology medicines); or 2) that the product, although authorised for marketing in all EU countries, has not (yet) been launched on the market in that country for that indication.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Table A C.6. Regulatory approval and coverage status of medicines used as *supportive care*

Active substance	ATC Code	ATC-4 Level	AUS	BEL	CHE	CHL	CYP	CZE	DEU	DNK	EST	FRA	GBR	GRC	HUN	IRL	ISR	JPN	KOR	LTU	LVA	MLT	NOR	SWE	USA
filgrastim*	L03AA02	colony stimulating factors																							
lipegfilgrastim	L03AA14	colony stimulating factors																							
pegfilgrastim	L03AA13	colony stimulating factors																							
dexamethasone*	H02AB02	corticosteroids																							
prednisolone*	H02AB06	corticosteroids																							
calcium folinate – leucovorin*	V03AF03	detoxifying agents for antineoplastic treatment																							
epoetin alfa	B03XA01	other antianaemic preparations																							
epoetin zeta	B03XA02	other antianaemic preparations																							

Note: Dark blue = not approved i.e. no marketing authorisation for this indication or not (yet) launched; medium blue = approved but not covered; light blue = approved and covered; white = no data provided.

* product/indication pair included in the WHO-EML (2019_[63]); † product/indication pair has been approved in the United States since 2014.

For EU members states (and Norway), when a medicine appears as “approved” in one country and “not approved” in another country, it might mean either 1) that the product has been approved before 1995 through national procedures (before systematic centralised marketing authorisation of all oncology medicines); or 2) that the product, although authorised for marketing in all EU countries, has not (yet) been launched on the market in that country for that indication.

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines.

Annexe D. OECD survey – cost sharing requirements

Table A D.1. Patient cost-sharing requirements for oncology medicines and medical services potentially including the administration of an oncology medicine

This table includes information on patient cost-sharing requirements for each country. It is based on information collected by the OECD as part of the *Health Systems Characteristics Survey* in 2012 and 2016. It has been updated with country responses to the 2019 survey focused on access to oncology medicines.

Country	Pharmaceuticals dispensed to patients for self-administration	Hospital inpatient care for cancer including the administration of a medicine	Outpatient specialist cancer services including the administration of a medicine	Exemptions or reductions of co-payments for some population groups	Annual cap for cost-sharing
Australia	Co-payment per item of AUD 41.00, reduced to AUD 6.60 for patients with concession card.	Free at the point of care for patients treated as public patients in public hospital. Patients treated as private patients in public or private hospitals have to pay a share of the cost, often paid by their private health insurance (with some services being partly funded via the Medicare system).	Outpatient specialist contacts are fully covered when provided in public hospitals, and generally covered with a 20% co-insurance when provided outside hospitals and financed by Medicare.	Co-payment reduced to AUD 6.60 for patients with concession card (low income). Reduction or exemptions for people with certain medical conditions and disabilities and for seniors; for children, war veterans and eligible Aboriginal and Torres Strait Islander patients.	When OOPs reach AUD 1486.80 (~1.8% of average wage), patients are entitled to concession card. After that, annual cap of AUD 316.80 (~0.4% of average wage) for concession card holders. Separate safety nets exist for services other than medicines. Cap on out-of-pocket costs for outpatient services covered by Medicare (i.e. services provided by GPs, specialists, private clinics and private emergency departments). Beyond an expenditure threshold, which varies with income and family situation (between approximately AUD 690 and 2200), Medicare pays 80% of OOP. People on low incomes qualify for the Safety Net at a lower threshold.

Country	Pharmaceuticals dispensed to patients for self-administration	Hospital inpatient care for cancer including the administration of a medicine	Outpatient specialist cancer services including the administration of a medicine	Exemptions or reductions of co-payments for some population groups	Annual cap for cost-sharing
Belgium	Cost-sharing ranging from 0% up to 100% according to drug category (drugs of high therapeutic value used in the treatment of severe diseases –diabetes, cancer – are free of charge but a co-payment is applied for other categories); patient status (preferential or not) and ex-factory price of the drug.	Co-payment per day, plus the costs of some non-reimbursable medical products or pharmaceuticals.	Co-payments between EUR 3.00 and EUR 12.00, depending on service type and patient status (GMD/preferential reimbursement). In general, patients pay the full price and are reimbursed afterwards.	Children, seniors and patients with certain medical conditions are exempted from co-payments for outpatient specialist care and inpatient care. Vulnerable populations are also exempted from co-payments and “up-front costs”.	Annual cap on cost-sharing. The amount depends on the annual income. Additional measures are foreseen for patients with preferential reimbursement, children (up to 18 years old) and chronically ill.
Canada	Varies across health insurance plans.	Free at the point of care.	Free at the point of care.	Most provincial and territorial governments fund a range of supplementary benefits that are not covered under the Canada Health Act for certain groups (incl. low-income residents). Outpatient-pharmaceuticals are covered in some provinces for all residents, while others focus on particular groups, incl. those on social assistance.	
Cyprus	Cancer therapy is provided free of charge to all patients whose annual income does not exceed EUR 135 000.00. Other patients cover all pharmaceutical expenditures by their own or from a private insurance.	Cancer therapy is provided free of charge to all patients whose annual income does not exceed EUR 135 000.00. Other patients cover all pharmaceutical expenditures by their own or from a private insurance.	Cancer therapy is provided free of charge to all patients whose annual income does not exceed EUR 135 000.00. Other patients cover all pharmaceutical expenditures by their own or from a private insurance.	Cancer therapy is provided free of charge to all patients whose annual income does not exceed EUR 135 000.00. Other patients cover all pharmaceutical expenditures by their own or from a private insurance.	
Czech Republic	Co-payment of any difference between pharmacy retail price and reimbursement price.	Free of charge.	Free of charge.	Exemptions for some groups of patients (patients receiving social benefits, children living in orphanages, <i>etc.</i>) in paying emergency/dental emergency visit fee. There are various age-related reductions of co-payments (annual caps) on partially reimbursed pharmaceuticals (see next column).	Annual caps on co-payments on partially reimbursed pharmaceuticals: ≤18 years – EUR 40 19–64 years – EUR 198 65–69 years – EUR 40 ≥70 years + 2 nd and 3 rd level of disability – EUR 20.

Country	Pharmaceuticals dispensed to patients for self-administration	Hospital inpatient care for cancer including the administration of a medicine	Outpatient specialist cancer services including the administration of a medicine	Exemptions or reductions of co-payments for some population groups	Annual cap for cost-sharing
Denmark	Deductible of DKR 980 beyond which co-insurance rate applies, diminishing stepwise as spending increases (50%, 25%, 15%).	Free at the point of care.	Free at the point of care.	Reduction or exemptions of co-payments on pharmaceuticals for people with certain medical conditions and disabilities and for seniors.	Annual cap for pharmaceuticals of DKK 4110 (~1% of average wage). Other services of medical diagnostic and curative care are virtually free of charge.
Estonia	For general prescription medicines, co-payment of EUR 2.50 per prescription, and co-insurance of at least 50%. For prescription medicines for chronic diseases, co-payment of EUR 2.50 per prescription, and co-insurance of 0 to 25%.	Co-payment of EUR 2.50 per day, up to 10 days per episode. Co-payments charged for above-standard accommodation.	Co-payment of EUR 5.00 for visits to specialists contracted with the health insurance fund, with a GP referral (exceptions are dermato-venereologist, gynaecologist and psychiatrist where no GP referral required). Visits without referral are not reimbursed. Specialists not contracted with health insurance determine their fees.	Reduced co-insurance (10%) on prescription medicines for chronic diseases for people with disability benefits or pensioners over 63 or children up to 16 years. Children under 18 exempted from co-payments for inpatient care. Children under 4 only pay EUR 2.50 per prescription medicine and no co-insurance.	Complementary reimbursement applies when patients cost-sharing is over EUR 100.00 per year (50% of costs exceeding the EUR 100.00 will be reimbursed) and 90% of costs exceeding EUR 300.00 per year will be reimbursed complementary).
France⁵⁶	Co-insurance of 0%, 35%, 70%, 85%, depending on drug category, plus co-payment of EUR 0.5 per item. For some medicines subject to reference prices, any difference between retail price and "reference price" is paid by the patient.	Co-insurance of 20%, not applicable for diagnostic or surgical procedures whose cost exceeds a certain threshold (EUR 120). Co-payment of EUR 20/day for acute in-patient care.	Co-payment of EUR 1 fee per consultation, plus cost-sharing of 30% with a GP referral, 70% otherwise. Patients may be exposed to extra-billing (allowed for 45% of private specialists). Patients pay the full price and are reimbursed afterwards.	Patients with malignant tumour or malignant affection of lymphatic or hematopoietic system are exempted from co-payments for all treatments related to this condition. People benefitting from a disability pension are fully covered for treatment of illness.	No.
Germany	Co-insurance of 10% of cost with a minimum of EUR 5 and a maximum of EUR 10 per item; co-payment cannot exceed the total drug price. For medicines subject to reference prices, any difference between retail price and "reference price" is paid by the patient.	Co-payment of EUR 10 /day, limited to 28 days/year.	Free at the point of care for patients with statutory health insurance and patients with selected private health insurance contracts.	Chronically ill and patients with disabilities have a lower cap on co-payments. Children are exempt from all co-payments.	Co-payments are capped at 2% of gross household income, reduced to 1% for the chronically ill.

⁵⁶ In France, more than 95% of the population is covered by complementary insurance, which often covers co-payments left by social health insurance.

Country	Pharmaceuticals dispensed to patients for self-administration	Hospital inpatient care for cancer including the administration of a medicine	Outpatient specialist cancer services including the administration of a medicine	Exemptions or reductions of co-payments for some population groups	Annual cap for cost-sharing
Greece	<p>Statutory co-insurance of 0%, 10% or 25% depending on drug category. Medicinal products for cancer and its consequences are fully covered.</p> <p>For medicines subject to reference prices, any difference between retail price and "reference price" is paid by the patient, up to 20€.</p> <p>1€ prescription fee is also applied in private pharmacies.</p>	<p>Free of charge for patients treated in public hospitals.</p> <p>High-cost medicinal products for cancer are provided free of charge from EOPYY to private clinics. Higher level of cost-sharing and potential extra-billing for patients in private hospitals.</p>	Free at the point of care for public providers.	<p>Some Chronically ill and patients with paraplegia, tetraplegia have exemptions for pharmaceutical cost-sharing. Patients belonging to low income/vulnerable groups are exempted from co-payments for pharmaceuticals.</p> <p>Women during pregnancy and lactation are exempted from co-payments on pharmaceuticals.</p>	
Hungary	<p>Co-payment of HUF 200 per pack.</p> <p>Any difference between retail price and "reference price" for products subject to reference pricing.</p>	Free at the point of care.	Free at the point of care.	Reduction or exemption for people with certain medical conditions and disabilities.	Entitlement to free pharmaceuticals for those whose medical expense exceeds 10% of the minimum pension (for households with income per capita < minimum pension = EUR 100 in 2010).
Ireland	<p>For medical card holders:</p> <p>Under the age of 70 years there is a prescription charge of €2 for each item, up to a maximum of €20 per month, for each person or family.</p> <p>Over 70 years, the prescription charge is €1.50 for each item, up to a maximum of €15 per month, for each person or family.</p> <p>For other groups, deductible of EUR 124 per family and per month before full reimbursement.</p>	<p>Free at the point of care for medical card holders and certain other categories. Co-payment of EUR 80 per day for public patients, capped at EUR 800 in any period of 12 consecutive months.</p>	Attendances at planned outpatient clinics in public hospitals are free at the point of care for public patients. Patients attending an emergency department are subject to a EUR 100 charge subject to a number of exemptions.	<p>Exemption for outpatient specialist care and pharmaceuticals for patients with certain medical conditions or disabilities (eligibility for Medical Card).</p> <p>40% of the population is entitled to the preferential status with no or lower co-payments for health services (Eligibility for Medical Card; Low-income, elderly, students, foster-care children etc.).</p> <p>Children and Students up to 25 are exempt from co-payments for acute inpatient care, outpatient specialist contacts and pharmaceuticals.</p> <p>Pregnant women are exempt for acute inpatient care and outpatient specialist contacts.</p>	Annual cap on inpatient care, primary care and pharmaceuticals, as indicated in relevant columns.

Country	Pharmaceuticals dispensed to patients for self-administration	Hospital inpatient care for cancer including the administration of a medicine	Outpatient specialist cancer services including the administration of a medicine	Exemptions or reductions of co-payments for some population groups	Annual cap for cost-sharing
Israel	<p>Patients pay a co-payment fee based on a three tier plan starting from a minimum of 17 ILS, to 10-15% of the public maximum price.</p> <p>Quarterly caps and discounts apply for certain target populations: elderlies, patients with HIV, Cystic Fibrosis, cancer, tuberculosis, etc.</p>	Free at the point of care.	Co-payment of approximately ILS 25 once every quarter.	<p>Reduction or exemptions for people with certain medical conditions and disabilities; for low-income patients and recipients of social benefits.</p> <p>Exemptions for holocaust survivors and those with disabilities due to active resistance to the Nazi regime, as well as victims of traffic accidents.</p>	Annual cap on inpatient and outpatient primary care.
Italy	<p>Co-payment per prescription or per package determined at regional level</p> <p>Patients wishing to get a higher-priced medicine (e.g. an originator brand) have to pay the difference between the reference price and the pharmacy retail price.</p>	Free at the point of care for patients treated as "public" patients in public and private hospitals.	Facilities and services included in the national health care entitlements (" <i>Livelli essenziali di assistenza</i> "(LEA)) have a co-payment of up to EUR 36.15 + EUR 10 fixed cost per prescription ⁵⁷ defined by the National legislation, which varies regionally (some regions do not apply it).	<p>Reduction or exemptions for people with certain medical conditions and disabilities and for seniors under designated income thresholds.</p> <p>Reduction or exemptions for low-income patients and patients receiving social benefits.</p> <p>Reductions or exemptions for children under a certain income threshold.</p>	
Japan	Co-insurance rate of 30% of costs.	Co-insurance of 30% of costs.	Co-insurance of 30% of costs.	<p>Co-insurance rates reduced to:</p> <ul style="list-style-type: none"> - 20% for infants and children before the school-age; - 20% for people aged 70-74 and 10% for people over 75 years, unless their income exceeds an annual threshold <p>The recipients of public assistance benefits are exempted from paying the co-insurance.</p>	Monthly cap depending on age and income.

⁵⁷ This extra-ticket ("super ticket") will be removed from September 2020, according to a recent decision that will be included in the budget law.

Country	Pharmaceuticals dispensed to patients for self-administration	Hospital inpatient care for cancer including the administration of a medicine	Outpatient specialist cancer services including the administration of a medicine	Exemptions or reductions of co-payments for some population groups	Annual cap for cost-sharing
Korea	Co-insurance of 30% (reduced to 5% for patients with severe diseases, incl. cancer).	Co-insurance of 20%, reduced to 5% for cancer-related medical services provided for severe diseases Co-insurance of 50% for meals, 10-50% for accommodation, depending on room type, 50-80% for oriental medical services, 30-90% for benefits with provisional coverage.	Co-insurance rate varies according to hospital type (60% for tertiary hospitals; 50% for general hospitals: (reduced to 45% in rural area); 40% in other hospitals (35% in rural area) Co-insurance of 30% in doctors' clinic. Co-insurance reduced to 5% for patients with cancer; except for 50-80% for oriental medical services, 30-90% on benefits with provisional coverage.	Co-insurance rates reduced for patients with severe illness (incl. cancer), see relevant categories. In addition, Medical Care Cost Support programmes provide subsidies to high-risk patients (disease included in a list of 132) whose income is below 300% of the established minimum cost of living, or who are enrolled in the nation-wide Medical Aid programmes. Seniors (>65) have reduced cost-sharing for primary care consultations. Children are exempt from co-payment for acute inpatient care, outpatient specialist care, and pharmaceuticals. Patients under a certain income threshold have reduced cost-sharing. Low income patients with cancer pay no co-insurance, except for meals (20%), benefits with provisional coverage (30-90%), and cost-sharing for accommodation (30-50% depending on room type), and for oriental medical services (30-80%).	Cap on annual cost-sharing, depending on income level (KRW 2 to 4 million, i.e. 5-10% of average annual wage).
Latvia	Co-insurance rate of 50%, 25% or 0% % for drugs used for chronic diseases and included in the Positive list. A co-payment of EUR 0.71 per prescription applies when the medicine is fully reimbursed. Any difference between retail price and reference price for products subject to reference pricing is paid by the patient.	Free at the point of care.	Free at the point of care.	No co-payment for children up to 18 years, vulnerable people, and asylum seekers, except any difference between retail price and reference price for products subject to reference prices. 50% reimbursement for all nationally registered prescription medicines (beyond those listed in the positive list) for children up to 24 months.	

Country	Pharmaceuticals dispensed to patients for self-administration	Hospital inpatient care for cancer including the administration of a medicine	Outpatient specialist cancer services including the administration of a medicine	Exemptions or reductions of co-payments for some population groups	Annual cap for cost-sharing
Lithuania⁵⁸	<p>No co-payment for medicines included in list A, used to treat specific conditions, including cancer.</p> <p>Other medicines (List B) are fully paid by patients, unless they are children, people with severe disabilities and people with specific conditions (no co-insurance) or for pensioners and people with less severe disabilities and reduced capacity to work (50% co-insurance).</p> <p>Patients may have to pay the difference between retail price and reimbursed price, with a cap of EUR 4.71 per prescription.</p>	Free for patients treated in public hospitals.	Free at the point of care for public providers.	No.	No.
Malta	No cost sharing. Free at point of care for all patients entitled according to the Social Security Act and Government Formulary List policies and entitlement protocols.	No cost sharing. Free at point of care for all patients entitled to free health care and according to the Social Security Act and Government Formulary List policies and entitlement protocols.	No cost sharing. Free at point of care for all patients entitled to free health care and according to the Social Security Act and Government Formulary List policies and entitlement protocols.	Not applicable.	Not applicable.
Norway	Anti-cancer drugs are normally financed by the hospital and free of charge for the patient. Co-insurance rate of 39% applies to pharmaceuticals financed through the National Insurance Scheme, capped to NOK 520 per prescription. Among anti-cancer drugs, only certain pharmacological treatments for breast and prostate cancer fall under the National Insurance Scheme.	Free at the point of care.	Outpatient care (tablets and injections) where the hospitals are responsible for treatment are free for the patient. Outpatient specialist consultations are subject to a co-payment of 375 NOK per visit (with annual ceiling of NOK 2369 in 2019).	Exemptions from and/or reductions of applicable co-payments under the National Insurance Scheme are available to children under 16 years of age, victims of occupational injuries and retirees with minimum income.	Annual cap (ceiling 1) of NOK 2369 (0.4% of average wage) in 2019 for the combination of expenses under the National Insurance Scheme (pharmaceuticals, consultations with primary care physicians, psychologists and psychiatrists, outpatient services in hospitals, physiotherapists, laboratory tests, x-rays).

⁵⁸ From the Lithuanian Health Profile (OECD/European Observatory on Health Systems and Policies, 2019) and survey response.

Country	Pharmaceuticals dispensed to patients for self-administration	Hospital inpatient care for cancer including the administration of a medicine	Outpatient specialist cancer services including the administration of a medicine	Exemptions or reductions of co-payments for some population groups	Annual cap for cost-sharing
Sweden	Deductible of SEK 1 150 (€ 105), beyond which co-insurance applies, diminishing stepwise (50%, 25%, and 10%). Patient annual OOP spending is capped to SEK 2 300.	Co-payment determined by each region, approx. SEK 100 per day.	Co-payment determined by each region, between SEK 230 and 350, with an annual cap on cost-sharing for outpatient care of SEK 1 150.	Those with certain medical conditions and disabilities; and children, are exempted for all cost-sharing. Low-income people are entitled to reduced hospital co-payments in some counties.	Annual cap for all cost-sharing requirements. Annual cap on co-payments for pharmaceuticals, set at SEK 2 300 (~0.5% of average annual wage).
Switzerland	Co-insurance of 10% up to an annual cap once the general deductible has been met. The deductible varies across insurance plans within a range of CHF 300 to CHF 2 500 per year. Co-payment is increased to 20% for off-patent drugs with cheaper (generic) alternatives.	Co-insurance of 10% after deductible, subject to annual cap. + Contribution to the costs of a hospital stay of CHF 15.00 per day. Children, young adults up to the age of 25 in training and women receiving maternity benefits are exempt from the hospital contribution.	10% cost-sharing after general deductible, with an annual cap.	Children under 18 have no deductible.	Patients' co-payments capped at CHF 700 (~0.8% of average wage) for an adult and CHF 350 for a child under 18 years.
United Kingdom (England only)	Co-payment of GBP 9 per prescription, no co-payment for cancer patients.	Free at the point of care.	Free at point of care.	The following categories are exempted from prescription fees: seniors and those affected with certain diseases, low-income people, children and pregnant women. Other medical diagnostic and curative services are typically free of charge. Low income groups receive further assistance via the NHS Low Income Scheme, which covers notably prescriptions, and health care related travel costs.	
United States⁵⁹	Cost-sharing requirements vary across health insurance plans. Medicare beneficiaries can get coverage for self-administered	Cost-sharing requirements vary across health insurance plans. Medicare beneficiaries can obtain coverage for medicines through	Cost-sharing requirements vary across health insurance plans. Medicare beneficiaries can obtain coverage for certain medicines and	Medicaid programmes may impose cost-sharing (co-payments, co-insurance and deductibles), which vary in nature and amount depending on income ⁶⁰ . Additionally, in Medicare Part D,	Most Medicare and Medicaid programmes have co-payments and deductibles, with exemptions for people who have paid for health expenditure above a certain threshold.

⁵⁹ Information on employer-sponsored health insurance extracted from (Claxton et al., 2019).

⁶⁰ <https://www.medicaid.gov/medicaid/cost-sharing/out-of-pocket-costs/index.html>

Country	Pharmaceuticals dispensed to patients for self-administration	Hospital inpatient care for cancer including the administration of a medicine	Outpatient specialist cancer services including the administration of a medicine	Exemptions or reductions of co-payments for some population groups	Annual cap for cost-sharing
Unites States (cont.)	<p>medicines through Medicare Part D. Part D sponsors offer plans with either a defined standard benefit or an "actuarially equivalent" value, and can also offer plans with enhanced benefits. The standard benefit in 2020 has a USD 435 deductible and 25% coinsurance up to an initial coverage limit of USD 4,020 (~6.4% of average wage) in total drug costs, followed by a coverage gap. In the gap, enrollees pay 25% coinsurance until their total true OOP spending reaches USD 6 350 (~10.1% of average wage). Thereafter, enrollees pay either 5% of total drug costs or USD 3.60/USD 8.95 for each generic and brand-name drug, respectively.</p> <p>In 2019, in employer-sponsored health insurance plans, 86% of covered workers face a deductible (USD 1,200 for single coverage). 91% of workers had plans with "tiered cost-sharing" for prescription drugs, with different average monthly co-payments across drug categories. In plans with 3 or more tiers of cost-sharing, co-payments were, on average: USD 11 for generics, USD 33 for "preferred drugs", USD 59 and USD 123 for drugs of the third and fourth tiers. In plans with co-insurance, the average rates were respectively 18%, 24%, 34% and 29% for the 1st, 2nd, 3rd and 4th tiers.</p>	<p>Medicare Part A. In 2020, Medicare Part A, enrollees face a deductible of USD 1,408 for each hospital admission and then no cost-sharing up to 60 days. Then, a co-payment of USD 352 per day applies up to the 90th day. Once in lifetime, patients can benefit from a per diem co-payment of USD 704 for an additional 60 days. After this, patients have to pay the full costs of inpatient care.</p> <p>In employer-sponsored health insurance plans, and after deductible, most workers face user charges when hospitalised (sometimes in addition to the general deductible): 66% pay co-insurance (20% on average); 14% pay fixed co-payments (USD 326 per hospital admission on average), 7% pay both types, and 5% per diem co-payments (USD 475 on average). 15% of insured have no additional cost-sharing after the general deductible has been met.</p>	<p>their administration through Medicare Part B. In 2019 Medicare, enrollees face a USD 185 annual deductible and then, generally 20% of Medicare-approved payment. Beneficiaries may also buy supplemental insurance coverage to help pay for Part B cost sharing amounts. In employer-sponsored health insurance plans, 72% of covered workers have a co-payment for a primary care office visit (USD 35 on average) and 20% have co-insurance (19% on average).</p> <p>In employer-sponsored plans, after deductible, 66% of patients pay fixed co-payment per visit (USD 40) and 26% pay co-insurance (19% on average). 5% pay no cost-sharing.</p>	<p>beneficiaries with lower incomes are eligible for low-income subsidies that significantly reduce patient cost-sharing.</p>	<p>In employer-sponsored health insurance plans, 99% of enrollees have cost-sharing caps. In individual plans, 29% of covered workers have a cap below USD 3,000 (~4.8% of average wage) and 20% a cap of USD 6 000 (~9.5% of average wage) or more.</p>

Note: OOP out-of-pocket payments, GP general practitioner, EOPYY National Organization for the Provision of Health Services (Greece), HIV human immunodeficiency virus

Source: Authors based on 2019 OECD survey on challenges in access to oncology medicines and (Auraaen et al., 2016^[84]). Average annual wages calculated based on 2018 data from OECD.stat <https://stats.oecd.org/Index.aspx?DataSetCode=MIN2AVE>

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