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Access to oncology medicines in EU and OECD countries

Thomas Hofmarcher,
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(*) Swedish Institute for Health Economics
(**) OECD, Directorate for Employment, Labour and Social Affairs, Health Division

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Executive Summary

Inequalities in patient access to cancer medicines and ensuring access to new cancer medicines are paramount challenges for healthcare systems. This working paper focuses on various aspects of inequalities in access to cancer medicines, covering the key stages along the life cycle of a medicine. The analysis draws mainly on findings of the section of the 2023 OECD Policy Survey on Cancer Care Performance relating to cancer medicines.

While more oncology medicines are being developed and approved, access inequalities persist

The number of approved cancer medicines has steadily increased over time. Between 2004 and 2011, the average annual number of approvals was close to four in the European Union and European Economic Area (EU/EEA) whereas 2021 and 2022 saw the approvals of 17 and 15 new cancer medicines, respectively. In addition, the number of approvals of extensions to new indications of existing medicines outnumbered the number of approvals of new medicines in recent years. The research pipeline in oncology signals that this development will probably continue in the near future.

Clinical trials and early access schemes offer patients an opportunity to receive new cancer medicines before regulatory approval and/or reimbursement approval. However, the number of clinical trials in oncology ranges from fewer than 2 trials to more than 10 trials per 100 000 inhabitants across the EU, with lower access in Eastern and Central European countries. Many countries use early access systems to improve access to novel cancer medicines despite limited/immature evidence on efficacy. Countries with early access schemes most often provide access on a named-patient basis, which typically only benefits a small share of clinically eligible patients.

Pricing and reimbursement arrangements significantly impact access to oncology medicines

In recent years, the rising prices of cancer medicines have led to increased spending on cancer care, posing affordability challenges even for affluent countries with publicly funded health systems. The budget impact of new medicines has become a significant factor in public coverage and reimbursement decisions, with most countries indicating its growing importance due to higher drug prices and the increasing number of new medicines. This makes it difficult for some countries to provide fast access to oncology medicines. In addition, many products come to the market with limited/immature evidence on efficacy and cost-effectiveness. Policies such as managed entry agreements (MEAs) to address uncertainty in coverage and/or pricing decisions for new cancer medicines/indications are growing in importance. The reimbursement of cancer medicines with a high clinical benefit varies substantially. Of a sample of indications with high clinical benefit in breast and lung cancer, Germany reported that all indications were covered, followed by the Netherlands (92%), and Bulgaria and Sweden (both 85%). Malta reimbursed no indications and Cyprus and Latvia reported small proportions of indications covered (both 31%). The time from European-wide marketing authorisation until national reimbursement/coverage ranged from around 100 days or less in Germany and Sweden to over three years in Cyprus, Latvia, and Lithuania.

The reimbursement of a companion diagnostic is not coupled to the reimbursement of a matching medicine in most countries. This can lead to a paradoxical situation in which a medicine is reimbursed but not its

companion diagnostic, necessitating patients to pay out-of-pocket or rely on funding from pharmaceutical companies. The lack of a joint reimbursement process for a medicine and its companion diagnostic may slow down the uptake of "personalised medicine" in clinical practice.

Policies to encourage the utilisation of generics and biosimilars vary across countries. Reference price systems for both generics and biosimilars are in place in a majority of countries, which can contribute to securing lower prices. The adoption of generics and biosimilars in clinical practice might be somewhat hampered by policies that do not allow or encourage substitution for reference medicines. A majority of countries do not mandate substitution for generics and few countries mandate it for biosimilars. This might deprive countries of achieving efficiencies in the rational use of medicines and sustaining medicine budgets.

Several policy options are available to aid payers and national competent authorities in enhancing patient access to cancer medicines.

Healthcare systems need to weigh the costs from investing in cancer medicines against the potential improvements in patient outcomes. An increased focus on spending on effective and cost-effective medicines should be considered. A formal health technology assessment (HTA), assessing both effectiveness and costs, should be conducted for all new medicines and extensions to new indications. In addition, the assessment of new medicines with a potentially high relative clinical benefit could be expedited. Not all new medicines are equally effective. Value frameworks, such as the ESMO-Magnitude of Clinical Benefit Scale, have been developed to support the process of HTA and to assist in rationalising reimbursement decisions.

Managed Entry Agreements (MEAs) may help patients to gain faster access to new cancer medicines despite limited/immature evidence on efficacy. Performance-based MEAs may seem more appealing because of their ability to link health outcomes to payments. However, their routine implementation for a wide range of medicines/indications is hampered by the additional administrative burden and/or lack of appropriate IT systems and staff. Functional systems where relevant data can be easily extracted from medical records and processed by healthcare payers would be needed. Purely financial MEAs might be the only feasible option for most countries and the majority of cancer medicines in the foreseeable future.

Addressing potential barriers that impede patient access to already reimbursed medicines and new cancer medicines is vital to enhance the quality of care. This includes, amongst others, ensuring adequate public budgets for reimbursed medicines, joint reimbursement decision of a medicine with its companion diagnostic, regular update of local clinical guidelines and protocols, continuous training of clinical staff, and adequate infrastructure and staff for diagnostic testing and treatment administration. Early access schemes using a named-patient approach create administrative burden to handle cases on a one-on-one basis and may only benefit well-informed patients or patients treated by certain physicians. A switch to a population-based system could be explored as it could contribute to reducing inequalities in access.

Increasing efficiency in the use of cancer medicines deserves greater attention. More effective measures are needed to stimulate competition between producers of generics and biosimilars and to control prices of reference medicines after loss of market exclusivity. This may create substantial budget headroom, which can be reinvested to increase access to new cancer medicines.

Résumé

Les inégalités dans l'accès des patients aux médicaments contre le cancer et l'assurance de l'accès aux nouvelles thérapeutiques sont des défis majeurs pour les systèmes de santé. Ce document de travail se concentre sur divers aspects des inégalités d'accès aux médicaments contre le cancer, couvrant les principales étapes du cycle de vie d'un médicament. Cette analyse s'appuie principalement sur les données de l'enquête de l'OCDE sur la performance des soins contre le cancer de 2023, plus particulièrement sa section relative aux médicaments contre le cancer.

Bien que de plus en plus de médicaments oncologiques soient développés et approuvés, les inégalités d'accès persistent.

Le nombre de médicaments contre le cancer approuvés a augmenté régulièrement ces dernières années. Entre 2004 et 2011, le nombre moyen annuel d'authorisation était autour de quatre dans l'Union européenne et l'Espace économique européen (UE/EEE), tandis que 2021 et 2022 ont vu respectivement l'approbation de 17 et 15 nouveaux médicaments contre le cancer. De plus, ces dernières années le nombre d'approbations d'extensions d'indications pour les médicaments existants a dépassé celui des authorisations de nouveaux médicaments. Le pipeline de recherche en oncologie indique que cette tendance se poursuivra probablement dans un avenir proche.

Les essais cliniques et les programmes d'accès précoce offrent aux patients la possibilité de recevoir de nouveaux médicaments oncologiques avant leur approbation réglementaire et/ou leur inclusion dans le panier de soins. Cependant, le nombre d'essais cliniques en oncologie varie de moins de 2 à plus de 10 essais pour 100 000 habitants à travers l'UE, avec un accès plus limité dans les pays d'Europe centrale et orientale. De nombreux pays utilisent des systèmes d'accès précoce pour améliorer l'accès aux nouveaux médicaments contre le cancer, en dépit de preuves d'efficacité limitées ou peu consolidées. Les pays dotés de systèmes d'accès précoce n'offrent le plus souvent cette opportunité que sur une base nominative, ce qui ne bénéficie généralement qu'à une petite part des patients éligibles sur le plan clinique.

Les arrangements en matière de prix et de remboursement ont un impact significatif sur l'accès aux médicaments oncologiques.

Ces dernières années, la hausse des prix des médicaments contre le cancer a entraîné une augmentation des dépenses de soins oncologiques posant des défis en matière d'accessibilité financière, même pour les pays aisés disposant de systèmes de santé financés par des régimes publics d'assurance maladie. L'impact budgétaire des nouveaux médicaments est devenu un facteur important lors des décisions d'inclusion dans le panier de soins, la plupart des pays soulignant son importance croissante en raison de l'augmentation des prix et du nombre des médicaments commercialisés. Pour certains pays, cette situation limite un accès rapide aux thérapies anti-cancéreuses. De plus, de nombreux produits arrivent sur le marché avec des preuves limitées ou non consolidées quant à leur efficacité et leur rapport coût-efficacité. Des mesures telles que les contrats d'accès au marché (Managed Entry Agreements - MEA) gagnent en importance pour réduire l'incertitude lors des décisions de couverture et/ou de tarification des nouveaux

médicaments et indications contre le cancer. De plus, le remboursement des médicaments contre le cancer même ayant un bénéfice clinique élevé peut varier considérablement. Parmi un échantillon d'indications avec un bénéfice clinique élevé dans les cancers du sein et du poumon, l'Allemagne rapportait que toutes les indications étaient couvertes, suivie des Pays-Bas (92 %), de la Bulgarie et de la Suède (toutes deux 85 %). A l'inverse, Malte ne remboursait aucune indication et Chypre et la Lettonie signalaient de faibles proportions d'indications couvertes (toutes deux à 31 %). Le délai entre l'autorisation de mise sur le marché à l'échelle européenne et l'éventuelle inclusion dans le pannier de soins variait d'environ 100 jours ou moins en Allemagne et en Suède à plus de trois ans à Chypre, en Lettonie et en Lituanie.

Dans la plupart des pays, le remboursement d'un test compagnon n'est pas couplé au remboursement du médicament correspondant. Ceci peut conduire à une situation paradoxale dans laquelle un médicament est remboursé mais pas son test compagnon, obligeant les patients à payer de leur poche ou à compter sur le soutien financier des entreprises pharmaceutiques. L'absence d'un processus de remboursement conjoint pour un médicament et son test compagnon peut en pratique freiner le déploiement de la médecine dite «personnalisée » en pratique clinique.

Les politiques visant à encourager l'utilisation des génériques et des biosimilaires varient d'un pays à l'autre. Les systèmes de prix de référence pour les génériques et les biosimilaires sont en place dans la majorité des pays Européens, ce qui contribue à tirer les prix vers le bas. L'adoption des génériques et des biosimilaires dans la pratique clinique reste en pratique freinée par une régulation n'autorisant pas ou n'encourageant pas la substitution des médicaments de référence. La majorité des pays n'oblige pas la substitution des génériques et ils sont encore moins à l'exiger pour les biosimilaires. Cette situation prive de nombreux pays de gains d'efficience non négligeables.

Plusieurs options politiques sont disponibles pour aider les payeurs et les autorités nationales compétentes à améliorer l'accès des patients aux médicaments contre le cancer.

Les systèmes de santé doivent soupeser les coûts consentis pour les médicaments contre le cancer au regard des résultats chez les patients. Il conviendrait d'accorder une attention renforcée aux dépenses portant sur des produits efficaces et coût-efficaces. Une évaluation formelle des technologies de santé (HTA), évaluant à la fois l'efficacité et les coûts associés, devrait être réalisée pour tous les nouveaux médicaments et les extensions à de nouvelles indications. De plus, l'évaluation des nouveaux médicaments présentant un bénéfice clinique relatif potentiellement élevé pourrait être accélérée. Tous les nouveaux médicaments n'ayant pas la même efficacité, des cadres de valeur, tels que l'échelle de magnitude du bénéfice clinique de l'ESMO, peuvent contribuer à l'évaluation des technologies de santé et par la même contribuer à rationaliser les décisions d'inclusion dans le panier de soins.

Les contrats d'accès au marché peuvent permettre un accès plus rapide aux nouveaux médicaments contre le cancer tout en réduisant les risques liés aux faibles niveaux de preuve quant à leur efficacité. Les contrats basés sur la performance peuvent sembler plus attrayants en raison de leur capacité à lier les résultats de santé aux coûts. Cependant, leur mise en œuvre systématique pour un large éventail de médicaments/indications est entravée par la charge administrative supplémentaire et/ou le manque de systèmes de données et de personnel dédié. Des systèmes où les données pertinentes peuvent être facilement extraites des dossiers médicaux et traitées par les payeurs de soins de santé seraient nécessaires. Les contrats d'accès purement financiers resteront sûrement la seule option réaliste pour la plupart des pays et pour la majorité des médicaments contre le cancer dans les années à venir.

S'attaquer aux obstacles potentiels qui entravent l'accès des patients aux médicaments déjà remboursés et aux nouveaux médicaments contre le cancer est essentiel pour améliorer la qualité des soins. Cela implique, entre autres, de garantir des budgets publics adéquats pour les médicaments remboursés, une décision conjointe de remboursement d'un médicament avec son test compagnon, la mise à jour régulière des recommandations cliniques et protocoles thérapeutiques, la formation continue du personnel clinique, ainsi qu'une infrastructure et un personnel adéquats pour les tests diagnostiques et l'administration de ces

traitements. Les programmes d'accès précoce sur base nominative créent une charge administrative pour traiter les cas individuellement et peuvent potentiellement ne bénéficier qu'aux patients bien informés ou traités par certains centres. Le passage à un système populationnel pourrait contribuer à réduire les inégalités d'accès à ces programmes.

L'amélioration de l’efficience dans l'utilisation des médicaments contre le cancer mérite une plus grande attention. Des mesures sont nécessaires pour stimuler la concurrence entre les producteurs de génériques et de biosimilaires et pour contrôler les prix des médicaments de référence après la perte de leurs exclusivités d’accès au marché. Ceci pourrait créer une marge budgétaire substantielle, pouvant être réinvestie pour accroître l'accès aux nouveaux médicaments contre le cancer.

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1 Introduction

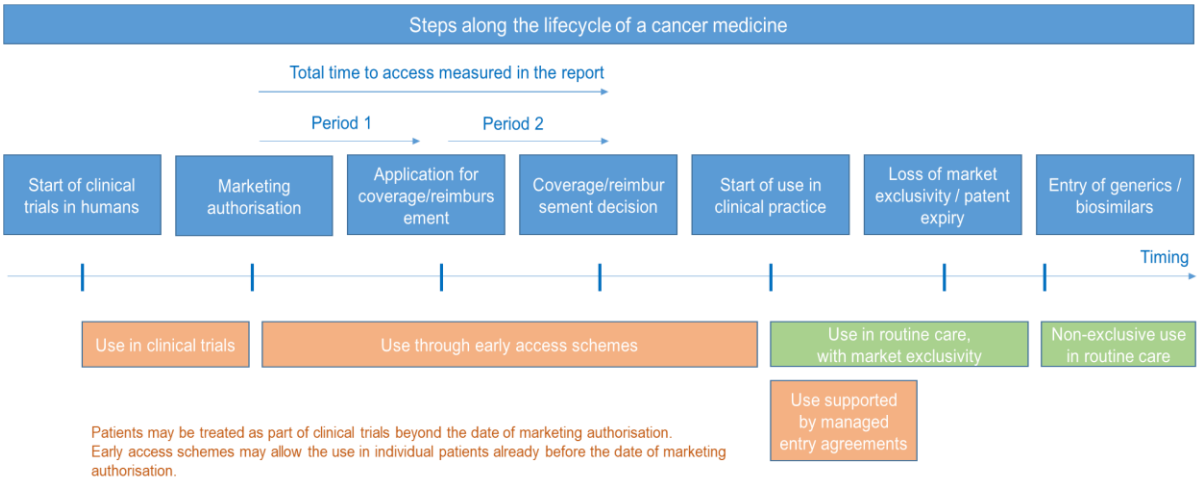
1. Cancer is a major public health concern in Europe. In 2022, there were an estimated 2.78 million new cancer cases in the 27 European Union Member States (EU27), plus Iceland and Norway (EU+2 countries), which is equivalent to about five new diagnoses every minute. By 2035, it is anticipated that cancer will be the leading cause of death in Europe.

2. Patient access to existing and new cancer medicines is vital to enhance the quality of care. Inequalities in access, especially to new medicines, between OECD countries have previously been documented (Chapman, Paris and Lopert, 2020[1]), and providing and sustaining access to new cancer medicines has become a concern even for most affluent countries around the world. In addition, novel challenges have emerged over the last decade, such as significant uncertainty surrounding the degree of clinical benefit offered by a new medicine at the time of market entry compared to the current standard-of-care, the valuation and pricing of medicines with multiple indications and with varying degrees of clinical benefit, and the valuation and pricing of on-patent medicines used in combination with other on-patent medicines. Policies and practices adopted by countries to address some of these challenges that are particularly salient in cancer medicines have already been described in a previous report (Chapman, Paris and Lopert, 2020[1]).

3. This working paper looks at various aspects of inequalities in access to cancer medicines drawing mainly on the results of the 2023 OECD Policy Survey on Cancer Care Performance covering the EU-27 countries and Iceland, Norway, and Switzerland (referred to as “EU/EEA/CH countries”) for questions relating to the availability of specific cancer medicines. Practices from other OECD countries (Australia, Canada, Mexico, New Zealand, USA) are also presented for more general questions not relating to the availability of cancer medicines. The focus is on cancer medicines only (i.e. not surgery and radiation therapy). Box 1.1 provides an overview of the different types of oncology medicines.

4. A new cancer medicine must go through several steps before it can reach patients; see Figure 1.1. This working paper discusses challenges and inequalities stemming from three of these steps – regulatory approval (section 2), pricing and reimbursement (section 3), and uptake and utilisation (section 4). Common challenges at the time of launch of new cancer medicines relate to uncertainties about the effectiveness in clinical practice and in comparison with standars of care, as well as about the cost-effectiveness due to high prices and unknown effectiveness. The broad use of new medicines in all clinically eligible patients may be restricted by constrained public health budgets (i.e., affordability), including at subnational level, as well as by required changes in patients’ clinical pathway, including biomarker testing and treatment administration, and training of clinical staff. This working paper also considers challenges with access to clinical trials, early access systems, and availability of generics and biosimilars. A number of general policy options to address some of the identified challenges and inequalities in access to cancer medicines are provided in the last section of the working paper (section 5).

Figure 1.1. Key stages along the life cycle of a cancer medicine



Source: Authors

Box 1.1. Types of cancer medicines[1]

The treatment of cancer comprises several modalities and depends on the cancer type and on the spread of the cancer in the body. Solid tumours are usually treated with a mix of surgery to remove the tumour, radiation therapy that uses high doses of radiation to kill cancer cells, and cancer medicines that stop cancer cells from growing by killing them or stopping them from replicating. Haematologic cancers, such as leukaemia and multiple myeloma, may be treated with cancer medicines and/or stem cell transplants where cells from the transplant donor attack cancer cells. The increased biological understanding of cancer and tumour growth has spurred the development of new classes of medicines with different mechanisms of action. An overview of broad classes of cancer medicines is provided below.

Chemotherapy has been used for decades and still today is a standard-of-care treatment in the treatment course of many cancer types. Traditional chemotherapeutic agents target the feature of rapid division of cancer cells. They kill cancer cells by interfering with cell division. Healthy cells in the body that are also dividing rapidly, such as in hair and in the gastrointestinal tract, may also be collaterally damaged, causing toxic side effects. Chemotherapy agents are typically administered intravenously in an outpatient hospital setting, every 2–6 weeks for a limited duration of around 3–6 months.

Hormone therapy (also known as endocrine therapy) targets hormones that cause certain cancers to grow, such as oestrogen in breast cancer (first medicine approved in 1977 in the U.S.) and testosterone in prostate cancer (discovered in 1941). Hormone therapy agents are typically administered as tablets and taken by patients at home every day for a duration of 1–3 years in prostate cancer and up to 10 years in breast cancer.

Targeted therapy (also known as molecularly targeted therapy) blocks specific molecules that are involved in the growth of cancer cells. The first agents were introduced at the end of the 1990s and are nowadays one of the main treatment options in various cancer types, especially at advanced disease stages. Targeted therapy agents are typically either administered intravenously in an outpatient hospital setting, every 1–6 weeks, or taken orally as tablets everyday by patients at home. The treatment duration in early-stage tumours after surgery is usually 1–3 years, and in metastatic tumours they are given until disease progression or unacceptable toxicity.

Immunotherapy helps the body's immune system to find and attack cancer cells. The first class of agents, called immune checkpoint inhibitors, were introduced in the beginning of the 2010s and are almost exclusively used in the treatment of solid tumours. The second class of agents, called CAR-T (chimeric antigen receptors) cell therapies, were introduced at the end of the 2010s and are used in various blood cancers. Immune checkpoint inhibitors are administered intravenously in an outpatient hospital setting, every 2–6 weeks for a limited duration of up to 6 months before surgery and up to 2 years after surgery in early-stage tumours, whereas they are typically given until disease progression or unacceptable toxicity in metastatic tumours. CAR-T cell therapies are one-time treatments and administered intravenously at specialised hospitals.

Apart from mechanisms of action, another common way of classifying cancer medicines is their molecule size and manufacturing process:

Small-molecule drugs are simple molecules, with a low molecular weight, produced by chemical synthesis. They include all chemotherapies, all hormone therapies, and many targeted therapies.

Biologics (large-molecule drugs) are complex molecules produced in living cell cultures. They include monoclonal antibodies on which all immune checkpoint inhibitors and many targeted therapies are based. They also include cell therapies such as CAR-T cell therapies. Biologics are more costly to

develop, harder to produce and imitate, and frequently have higher prices than small-molecule drugs (Blackstone and Joseph, 2013[2]; Makurvet, 2021[3]). While strictly identical copies can be made of a small-molecule drug, for a biologic it is only possible to ensure highly similar but not identical copies. Once a new medicine has lost its patent, other pharmaceutical producers can manufacture the same chemical substance in the case of small-molecule drugs or a highly similar molecular version in the case of biologics. A copy of a small-molecule drug of a producer other than the original producer is called a **generic**. A copy of a biologic is called a **biosimilar** (or follow-on biologic).

[1] See https://www.cancer.gov/about-cancer/treatment and https://www.cancer.gov/research/progress/250-years-milestones, accessed May 2023.

2 Regulatory approval of cancer medicines

2.1 Approval of new cancer medicines

5. The first step for patient access to new cancer medicines is the approval by a regulatory body. Regulatory agencies evaluate the safety, quality, and efficacy of new medicines before granting marketing authorisation (regulatory approval) in their jurisdiction. In the EU/EEA, the European Medicines Agency (EMA) has been responsible for the scientific evaluation of so-called centralised marketing authorisation applications of medicines since 1995. Since 2004, all new cancer medicines must follow this centralised procedure to receive marketing authorisation for the EU/EEA.[2]

There has been a marked increase in the number of approved cancer medicines in the past two decades

6. Between 2004 and 2022, 152 new cancer medicines were granted centralised marketing authorisation by the EMA (European Medicines Agency, 2023[4]); see Figure 2.1. There has been a marked increase in the number of approved medicines each year. Three distinct periods are noticeable. Between 2004 and 2011, the average annual number was close to four. Around ten new medicines per year were approved between 2012 and 2020. 2021 has been an exceptional year with 17 approvals of new cancer medicines, followed by 15 approvals in 2022. The number of recent approvals differs greatly by drug class. Of the 42 approvals of new cancer medicines between 2020 and 2022, 34 approvals (81%) concerned targeted therapies (including anti-body drug conjugates and bi-specific T-cell engagers), 7 approvals (17%) concerned immunotherapies, and one approval was for a hormone therapy. The latest new chemotherapy was approved in 2016. These trends are also observed in the United States, as documented in an analysis of US Food and Drug Administration (FDA) approvals between 2000 and 2022 (Scott et al., 2023[5]).

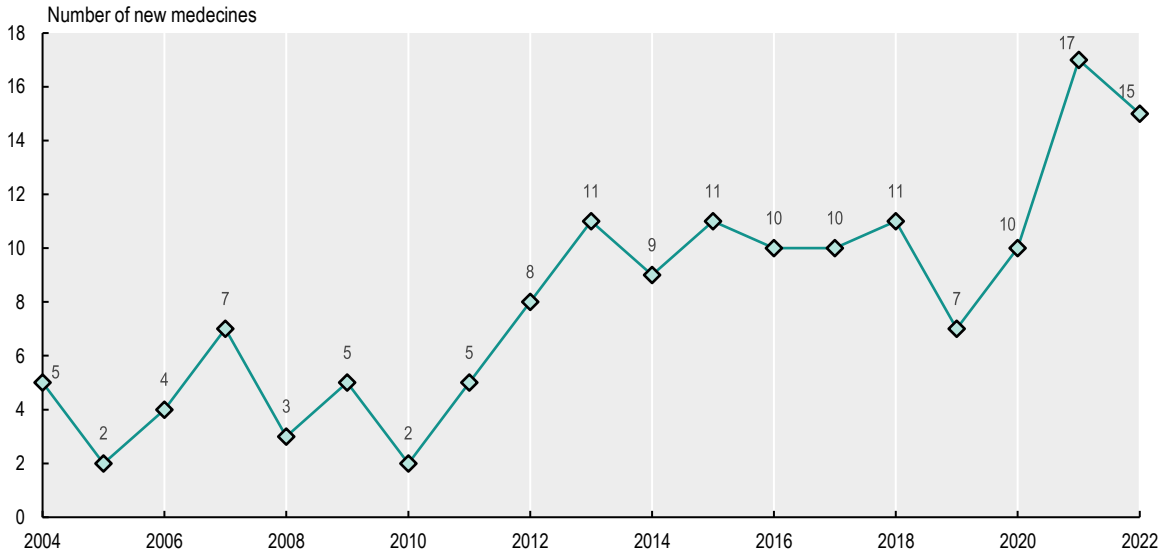
Extensions to new indications are also on the rise

7. The sole consideration of approvals of new cancer medicines only partly captures the changing treatment possibilities for patients. Extensions of the use of existing medicines to new indications (i.e., new patient groups) are common. These extensions are also subject to approval by the FDA and the EMA in the United States and the EU/EEA countries, respectively. In recent years, the number of extensions to new indications always outnumbered the number of approvals of new medicines. Between 2020 and 2022, there were 73 approvals of extensions of existing medicines by the EMA, of which 45% concerned

[2] See https://health.ec.europa.eu/medicinal-products/legal-framework-governing-medicinal-products-human-use-eu/authorisation-procedures-centralised-procedure_en, accessed June 2023.

immunotherapies, 45% targeted therapies, 4% combinations of immunotherapies with targeted therapies, and the remaining 6% pertained to other medicines.[3]

Figure 2.1. Annual number of new cancer medicines approved by the EMA, 2004–2022



Notes: Medicines used in cancer patients in the Anatomical Therapeutic Chemical (ATC) groups L01, L02, and L04 were included. Radiopharmaceuticals in ATC group V were not included. Medicines with identical active substances have only been included at their first instance of marketing authorisation. Six medicines are included that had their authorisation withdrawn after initial approval.
Source: Authors' calculations based on data from the EMA (European Medicines Agency, 2023[4]).

2.2 Approval of biosimilars and generics of cancer medicines

Approval processes of generics and biosimilars differ substantially

8. After the end of a period of market exclusivity for new medicines, biosimilars and generics can be marketed upon obtaining regulatory approval. Generic medicines contain the same active substance(s) as the reference medicine (i.e. the same chemical molecule). In the United States, the FDA approves all generic medicines, which, among others, need to scientifically demonstrate that they are bioequivalent (i.e., performs in the same manner) to the reference medicine.[4] In the EU/EEA countries, there are different routes to approve generic medicines, including national, mutual recognition, decentralised, and centralised authorisation processes. The latter is carried out by the EMA and may only be used for applications if the reference medicine was centrally authorised or if the generic medicine provides a significant innovation or advantage for patients.[5] Applications of generic medicines to the EMA usually only need to provide information on the quality of the medicine and demonstrate that the generic medicine produces the same levels of the active substance in the human body as the reference medicine. According to the EMA annual

[3] Authors' calculations based on recommendations of the Committee for Medicinal Products for Human Use (CHMP) of the EMA, see https://www.ema.europa.eu/en/committees/chmp/chmp-agendas-minutes-highlights, accessed June 2023.

[4] See https://www.fda.gov/drugs/types-applications/abbreviated-new-drug-application-anda, accessed June 2023.

[5] See https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/generic-hybrid-medicines, accessed June 2023.

report 2022, 90% of the medicines, mainly generic medicines, entering the EU/EEA market were approved through the national, mutual recognition, or decentralised process (European Medicines Agency, 2023[6]).

9. Biosimilars, which are copies of biologic medicines, require more thorough evaluation to obtain regulatory approval than generics. Biosimilars are highly similar to an existing reference biologic medicine. In the United States, the FDA approves all biosimilars, and evaluates them in terms of safety, purity, and potency (safety and effectiveness) (U.S. Food and Drug Administration, 2022[7]). In the EU/EEA countries, the EMA approves nearly all biosimilars, and approval through the centralised procedure is mandatory for all biosimilars used in the treatment of cancer (European Medicines Agency & European Commission, 2019[8]). The EMA evaluates biosimilars according to the same standards of quality, safety, and efficacy as all biologic medicines (European Medicines Agency & European Commission, 2019[8]). Both the U.S. FDA and the EMA maintain that a biosimilar may only require efficacy data in one indication for the marketing authorisation to be extrapolated to all indications of the reference medicine (European Medicines Agency & European Commission, 2019[8]; U.S. Food and Drug Administration, 2022[7]).

Biosimilars for three cancer medicines have been approved in Europe so far and more are expected to be approved in the current decade

10. Until 2023, the EMA had approved biosimilars for three cancer medicines (not including supportive medicines).[6] These are biosimilars for rituximab (first approval in 2017; reference medicine approved in 1998) used in the treatment of lymphoma and leukaemia, trastuzumab (first approval in 2017; reference medicine approved in 2000) used in the treatment of breast cancer and gastric cancer, and bevacizumab (first approval in 2018; reference medicine approved in 2005) used in the treatment of several cancer types such as colorectal cancer and ovarian cancer. In 2012 and 2015, these three products were the most sold cancer medicines in terms of sales value (based on list prices without considering confidential rebates) in Europe, accounting for 27.4% and 23.6%, respectively, of the sales value of all cancer medicines (Hofmarcher et al., 2019[9]). Despite evergreening strategies (Kirshner et al., 2024[10]), the current decade will see the loss of market exclusivity of an increasing number of biologics in oncology, as ten biologics with current active marketing authorisation for cancer treatment were approved by the EMA between 2011 and 2015.[7]

2.3 Policy issues

11. Regulatory bodies worldwide were faced with an increasing number of applications of new cancer medicines in the recent two decades. Extensions of indications of already existing cancer medicines add to the workload. This development will probably continue in the near future. In 2022, oncology was the therapeutic area with the most clinical trial activity, accounting for 40% of trial starts, and comprising 2,331 products in phase I to III trials (IQVIA, 2023[11]; IQVIA, 2023[12]); see also Box 2.1. This represented around a doubling of the number of oncology products being trialled compared to 2012 (IQVIA, 2023[11]; IQVIA, 2023[12]). Similarly, a previous analysis by the OECD also indicated that oncology accounted for the largest proportion of product-indication pairs that entered pre-clinical or clinical development in every year since 2011, and its proportion has increased steadily, from 27% of all product-indication pairs in 2011 to 40% in 2021 (Keelara et al., 2023[13]).

[6] Authors' calculations based on EMA approvals https://www.ema.europa.eu/en/medicines/download-medicine-data, accessed April 2023.

[7] Authors' calculations based on EMA approvals https://www.ema.europa.eu/en/medicines/download-medicine-data, accessed April 2023.

Box 2.1. Clinical trials of cancer medicines[8]

New cancer medicines go through a series of clinical trials in humans before the pharmaceutical company can apply for regulatory approval.

- Phase I: Typically involves 15–30 patients. The purpose is to find a safe dose, to decide how the medicine should be administered (by mouth, in a vein, etc.), to see how the medicine affects the human body and fights cancer.
- Phase II: Typically involves <100 patients. The purpose is to determine if the medicine has an effect on a certain cancer and to see how the medicine affects the body and fights cancer.
- Phase III: Typically involves >100 patients. The purpose is to compare the medicine with the current standard treatment.

If a new medicine is successful in one phase, it will proceed to further testing in the next phase. An analysis of clinical trials conducted in oncology between 1st January 2000 and 31st October 2015 found a success rates of 3.4% of medicines entering phase I studies with eventual regulatory approval (Wong, Siah and Lo, 2019[14]).

Most new oncology medicines are first marketed in the United States

12. Pharmaceutical companies most often apply first in the United States for regulatory approval. An analysis of cancer medicines approved between 2007 and 2020 found that the FDA was the first regulator to approve in 80% of cases (Hwang et al., 2022[15]). Medicines are typically approved later in the EU/EEA. Different studies of approvals of different samples of cancer medicines have found a mean or median delay of around 7–8 months of EMA approvals compared to FDA approvals in the last decade (Jacquet et al., 2021[16]; Lythgoe et al., 2022[17]). An analysis of 113 medicines (including non-oncology medicines) authorised by the FDA in 2015–2017 found that the greater use of expedited programmesby the FDA and administrative time at the European Commission mainly explain the later authorisation in the EU/EEA (Joppi et al., 2020[18]).

Initiatives are being discussed to accelerate approval of oncology medicines worldwide

13. Proposed revisions of the EU pharmaceutical legislation, put forward by the European Commission in April 2023, aim to accelerate procedures of the EMA and reduce authorisation times for medicines (see Box 2.2).[9]

14. Several international regulatory bodies have also recently started to cooperate for the authorisation process of promising new cancer medicines. Project Orbis was initiated by FDA in the United States in 2019 to provide a framework for concurrent submission and review of cancer medicines by international regulatory bodies.[10] Besides the FDA, the initiative includes the regulatory bodies of Australia, Brazil, Canada, Israel, Singapore, Switzerland, and the United Kingdom as of April 2024. This collaboration may allow cancer patients to receive earlier access to new medicines in countries outside the United States.

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[8] See https://www.cancer.gov/about-cancer/treatment/clinical-trials/what-are-trials/phases, accessed September 2023.

[9] See https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/reform-eu-pharmaceutical-legislation_en, accessed June 2023.

[10] See https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis, accessed April 2024.

Box 2.2. The proposed EU pharmaceutical legislation

In April 2023, The European Commission published a proposal to revise the existing EU pharmaceutical legislation. One of the many objectives of the revision is to simplify the regulatory framework and enable faster authorisation of innovative medicines. Currently, the regulatory framework mandates that upon submission of a valid application, the evaluation by the Committee for Medicinal Products for Human Use (CHMP) of the EMA takes up to 210 days, at the end of which the CHMP must issue a scientific opinion on whether the medicine may be authorised or not (European Medicines Agency, 2015[19]). This opinion is then transmitted to the European Commission, which has the ultimate authority for granting the marketing authorisation within 67 days after receipt of the CHMP opinion (European Medicines Agency, 2015[19]).

The proposal[11] from the European Commission from April 2023 notes that *"… for its assessment, EMA will have 180 instead of 210 days. For the authorisation, the Commission will have 46 instead of 67 days. This will help to reduce the current average of around 400 days between submission and market authorisation. For the assessment of medicines that are of major public health interest, EMA will only take 150 days … ."*.

In March 2024, the Committee on the Environment, Public Health and Food Safety (ENVI) of the European Parliament adopted its proposals for the EU pharmaceutical legislation.12 No changes to the Commission's proposed shorter timelines have been made. In April 2024, the European Parliament voted in favour of the adopted text by the ENVI.13 However, an agreement with the Council of the EU will have to be reached in the new term of the Parliament and the Commission after the EU elections in June 2024.

[11] See https://ec.europa.eu/commission/presscorner/detail/en/qanda_23_1844, accessed September 2023.

[12] See https://www.europarl.europa.eu/news/en/press-room/20240318IPR19419/eu-pharmaceutical-policy-meps-support-comprehensive-reform, accessed April 2024.

[13] See https://www.europarl.europa.eu/news/en/press-room/20240408IPR20308/parliament-adopts-its-position-on-eu-pharmaceutical-reform, accessed April 2024.

3 Pricing and reimbursement of cancer medicines

15. The second step for patient access to new cancer medicines in countries with predominantly public healthcare systems is pricing and reimbursement decisions by the national/regional healthcare payer(s). This typically requires an application by the pharmaceutical manufacturer for a specific indication that has received regulatory approval. The subsequent process of the assessment of the application varies between countries and may involve different criteria such as the medicine's effectiveness, cost-effectiveness, and budget impact. Different approaches on how to handle uncertainties in the evaluation of these criteria might also be applied across countries. All these factors may contribute to inequalities in the availability and coverage of new medicines between countries.

3.1 Pricing, reimbursement and budget impact

European countries rely on health technology assessment to inform reimbursement decisions

16. Nearly all EU/EEA countries, except for Cyprus and Slovenia, have established a health technology assessment (HTA) agency to inform decision-making in the pricing and reimbursement of a new medicine/indication (World Health Organization, 2018[20]; OECD/European Observatory on Health Systems and Policies, 2021[21]). Depending on the country, the HTA agency either makes the formal reimbursement decision (e.g., the Dental and Pharmaceutical Benefits Agency in Sweden for outpatient medicines) or issues a recommendation for reimbursement to the decision-making body (e.g., the National Centre for Pharmacoeconomics issues a recommendation to the Health Service Executive in Ireland). A positive decision means that patients covered by the public payer can access the new medicine.

17. In most EU/EEA countries, reimbursement decisions are made at the national level (Chapman, Paris and Lopert, 2020[1]). However, a few countries take more decentralised approaches, which can create inequities in access within a country. In the Nordic countries and Italy, funding for inpatient or outpatient cancer medicines may be a regional responsibility, with reimbursement decisions made at this level. Regional administrations may have variable capacity—both administrative, technical and financial—to respond to the pressures that cancer medicines pose to their systems. This can create significant disparities in access across populations.

18. The comprehensiveness of the HTA process differs from country to country and it may be applied systematically to all new medicines/indications or only to a subset (World Health Organization, 2018[20]). Key elements of a comprehensive HTA are the analysis of the additional health benefit (relative effectiveness) as well as the relative costs compared to the current standard of care. The joint evaluation of both incremental therapeutic benefit and incremental costs is required to establish the cost-effectiveness (value-for-money) of a new medicine/indication. An HTA that includes the evaluation of cost-effectiveness helps to weigh the costs from investing in different areas of care against the potential improvements in

patient outcomes. This enables evidence-based decision-making in cancer care and in healthcare more generally.

Pricing of new medicines typically involves the use of a reference price and subsequent negotiations

19. Pricing policies have been defined as "regulations and processes used by government authorities to set the price of medicines to exercise price control" by the WHO (World Health Organization, 2018[20]). Countries generally use a mix of policy instruments to determine or negotiate the prices of new products. Virtually all countries in the EU/EEA rely on external reference pricing at some point of their negotiation process; see Table 3.1. This practice involves the use of prices of a medicine in a pre-defined set of countries to calculate a national reference price for the medicine. The calculated national reference price is typically used as a starting point to initiate price negations with the pharmaceutical manufacturer during the pricing and reimbursement process. The final negotiated price may be confidential, which makes it difficult to compare the actual prices of cancer medicines across countries. In Sweden and the United Kingdom, the submitted price by the pharmaceutical manufacturer for the medicine is used as a direct input in the HTA process, and it may also be subject to negotiations during this process.

Table 3.1. Pricing policies of medicines in selected countries in Europe (in 2018)

Pricing policy	Country
External reference pricing being used at least for some medicines	Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Switzerland
Other pricing policy	Sweden, United Kingdom

Source: (World Health Organization, 2018[20]).

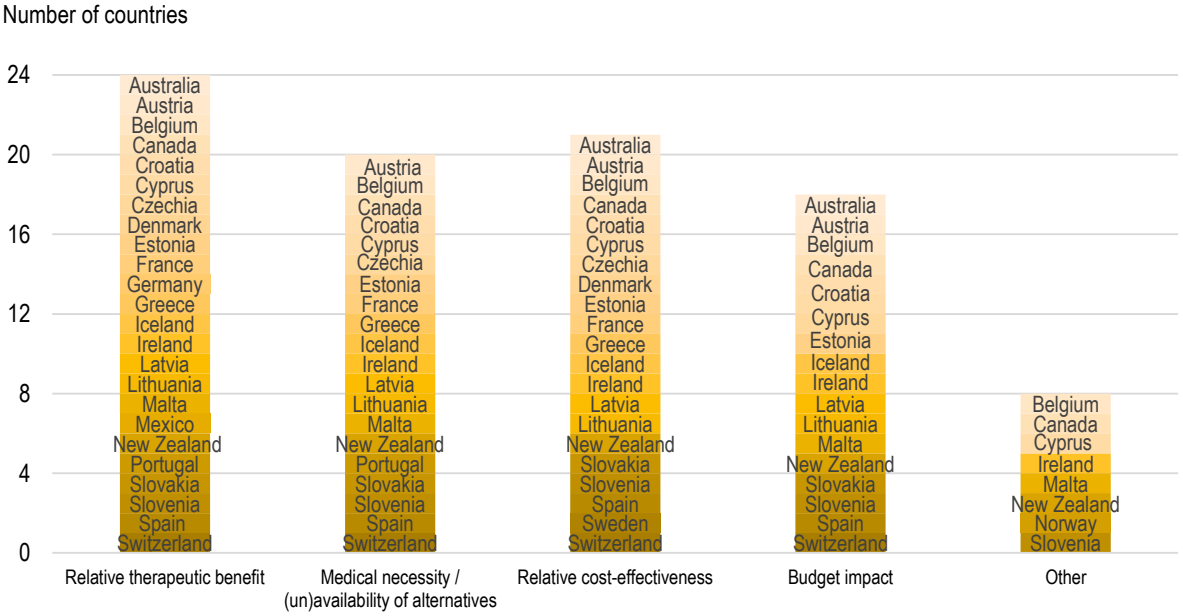
Relative therapeutic benefit is the criterion most frequently used to support reimbursement decisions of cancer medicines

20. As noted above, the reimbursement decision of new cancer medicines may rely on various criteria. Respondents to the 2023 OECD Policy Survey on Cancer Care Performance were asked what criteria, if any, are used to decide on publicly-funded coverage/reimbursement of new cancer medicines/indications, separately for outpatient medicines (see Figure 3.1) and inpatient medicines (see Figure 3.2).

21. The most common criterion was the relative therapeutic benefit in both cases. This was closely followed by medical necessity / (un)availability of treatment alternatives as well as two cost-related criteria, relative cost-effectiveness and budget impact. Additional criteria that are applied by some countries are the price and requested reimbursement level (in Belgium), the number of EU member states in which a medicine is already reimbursed (for inpatient medicines in Croatia), the combination of "seriousness, usefulness, and resource use" (in Norway), ethical considerations such as orphan status (in Slovenia). In several countries, decision criteria applied to outpatient and to inpatient cancer medicines are different. In Austria, outpatient medicines must fulfil all four criteria shown in Figure 3.1, whereas inpatient medicines are reimbursed upon a proposal from a hospital, based on medical necessity. Similarly, in Czechia, inpatient medicines are covered automatically from specific budgets that are negotiated between healthcare providers and payers (i.e., insurance companies), while outpatient medicines must fulfil all four criteria shown in Figure 3.1.

Figure 3.1. Criteria for decision on public coverage/reimbursement for outpatient cancer medicines

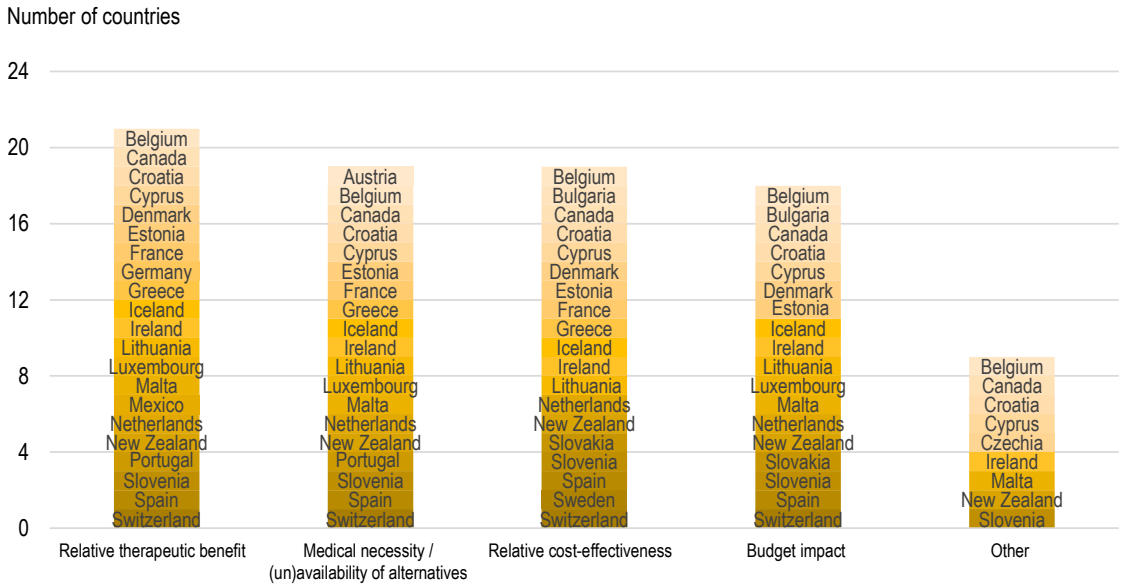
Based on responses from 28 countries (multiple options possible per country).



Notes: In the Netherlands, cancer medicines are only available in the inpatient setting. No response provided by Bulgaria and Luxembourg.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

Figure 3.2. Criteria for decision on public coverage/reimbursement for inpatient cancer medicines

Based on responses from 28 countries (multiple options possible per country).



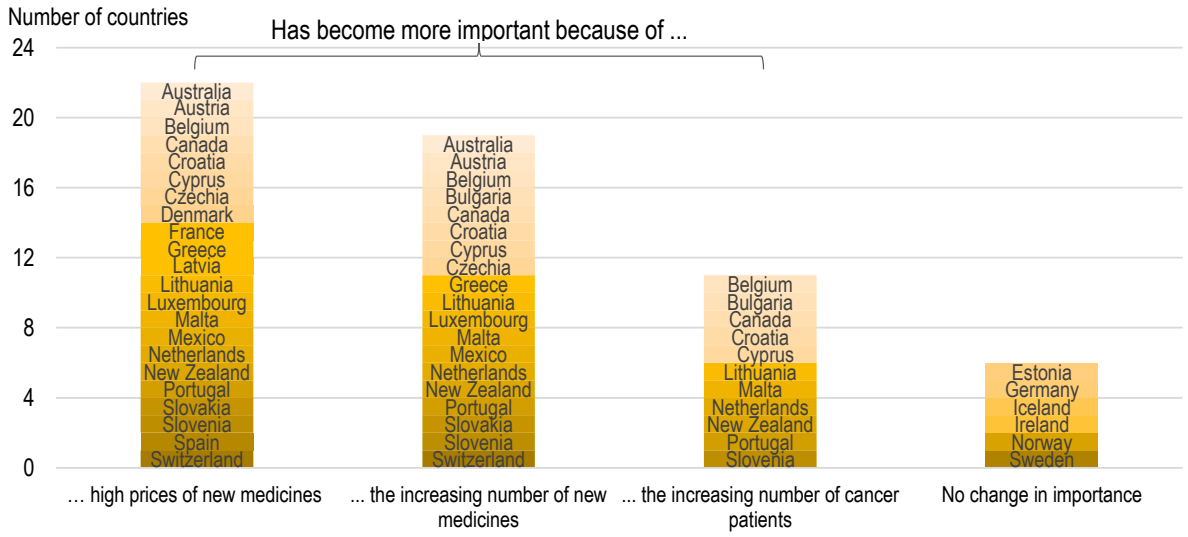
Notes: No response provided by Australia, Latvia, and Norway.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

The budget impact of new cancer medicines is increasingly influencing reimbursement decisions

22. The most recent years and decades have witnessed rising prices of individual cancer medicines (Chapman, Paris and Lopert, 2020[1]) and rising expenditure on cancer medicines as a whole, both in absolute terms and in relative terms of total spending on cancer care (Hofmarcher et al., 2019[9]). This might create an affordability challenge even for more affluent countries, in particular for publicly funded health systems that operate on constrained budgets (Vogler, 2021[22]; World Health Organization, 2018[23]). The budget impact of new medicines already appears to be an important criterion in the public coverage/reimbursement decisions as presented above. In addition, respondents to the 2023 OECD Policy Survey on Cancer Care Performance were also asked whether the budget impact of new medicines has been become more important for public coverage/reimbursement decisions in recent years; Figure 3.3. Most countries indicated that the budget impact is increasingly influencing their coverage/reimbursement decisions. They also indicated that there are various reasons, most importantly rising prices of new medicines and the increasing number of new medicines. The rising number of cancer patients was also cited as a contributing factor in a number of countries. Only six countries did not indicate an increasing importance of the budget impact for coverage/reimbursement decisions (Estonia, Germany, Iceland, Ireland, Norway, and Sweden). However, this does not mean that the budget impact is not a concern in these countries. In Estonia, the importance of the budget impact has remained at the same level, yet the impact of higher prices of medicines on the financing of the budget has increased. In Iceland, the budget impact has been important for a long time, especially in the aftermath of the financial crisis in 2008 but has become less important - yet remaining important overall – as the country recovered financially.

Figure 3.3. Importance of the budget impact of new cancer medicines for public coverage/reimbursement decisions in the last five years

Based on responses from 28 countries (multiple options possible per country).



Notes: The underlying survey question asked about changes in the importance of considerations of the budget impact within the last five years.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

3.2 Approaches to address uncertainties

23. The provision of evidence-based care requires reliable information on the performance of a new medicine in clinical practice. At the time of the assessment by the pricing and reimbursement body, a full picture of the effects of a new medicine might not yet be available. Most assessments use data from clinical trials, which inherently involve uncertainty about the effects in clinical practice, i.e., the difference between the efficacy of a medicine and the effectiveness of a medicine. This creates a trade-off for public healthcare payers between providing early patient access to new, promising medicines and ensuring solid evidence about the value to patients and society (Eichler et al., 2015[24]; Eichler et al., 2019[25]).

Uncertainty in the assessment of clinical benefit is particularly high for cancer medicines

24. Clinical data used for regulatory approval of cancer medicines are not always based on large-scale phase III randomised controlled trials (RCTs). Instead, they might rely on phase II trials and/or single-arm trials for various reasons, such as small patient populations (Naci et al., 2019[26]). An analysis of cancer medicines/indications approved by the EMA from 2010 to 2019 found that out of 199 approvals, 159 (80%) were based on at least one RCT and the remaining 40 (20%) were not supported by an RCT, but 9 of those approvals were followed by a post-approval RCT (Farina et al., 2021[27]). Another challenge is that the effects on patients' health in clinical trials are often measured with surrogate endpoints, such as progression-free survival in the metastatic treatment setting, instead of with the "real" clinical endpoint which is overall survival (Naci et al., 2019[26]). Many review studies have tried to systematically examine the efficacy of cancer medicines approved by the EMA. An analysis of 48 medicines for 68 indications approved in 2009–2013 showed that most medicines were approved without evidence of benefit on overall survival (65% of all indications) or quality of life (90%), and after a post-marketing period of at least three years, no conclusive evidence on these outcomes had emerged for 49% of all indications (Davis et al., 2017[28]). Of medicines approved in 2009–2015 with initially ambiguous benefit-risk profiles, one third of the medicines has been found to lack evidence on improved overall survival after a post-marketing period of at least three years by another study (Grössmann et al., 2019[29]). An analysis of all 132 EMA-approved indications for solid tumours between 2015 and 2020 found that overall survival represented the primary endpoint in clinical studies in 39% of indications only, the median overall survival increase between the treatment arm and the control arm was 2.81 months, and if quality of life was reported, for most of indications (62.5%) there was no significant difference between the treatment arm and the control arm (Falcone et al., 2022[30]).

25. Uncertain or incomplete clinical data at the time of regulatory approval do not imply that a medicine is not effective or cost-effective, but it complicates a fair and reliable evaluation of the medicine during the HTA process. Different policies and approaches exist to manage uncertainties in clinical benefit, cost-effectiveness, and budget impact; see recent OECD reports for an extensive description of managed entry agreements (MEAs)[14], in particular (Chapman, Paris and Lopert, 2020[1]; Wenzl and Chapman, 2019[31]). The aim of these policies and approaches is to share the uncertainty (and associated risk) between healthcare payers and marketing authorisation holders. However, different countries might place a greater

[14] MEAs have been very broadly defined by (Klemp et al., 2011[83]) as "*arrangement[s] between a manufacturer and payer/provider that enable access to (coverage/reimbursement of) a health technology subject to specified conditions. These arrangements can use a variety of mechanisms to address uncertainty about the performance of technologies or to manage the adoption of technologies in order to maximize their effective use, or limit their budget impact." (p.79)*. MEAs fall into two groups, either they are financial (i.e. secret discounts/rebates between the payer and the marketing authorisation holder), or they are performance-based, e.g. imposing payment-by-result. Performance-based agreements may also have a financial objective, but contingent on the performance of the technology (Wenzl and Chapman, 2019[31]).

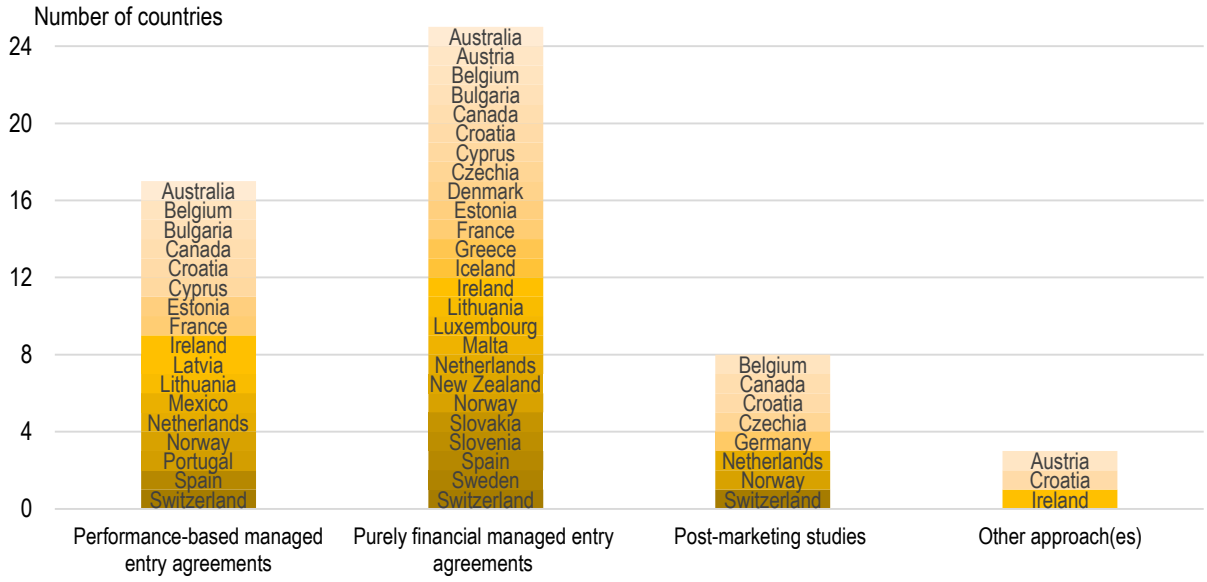
weight on particular uncertainties. For example, a study of MEAs in Bulgaria, Croatia, Czechia, Hungary, Poland and Romania showed that the main role of MEAs and other related policies was to limit the budget impact of new medicines, whereas uncertainty about outcomes and appropriate utilisation seemed to be of lower priority (Rotar et al., 2018[32]).

Financial managed entry agreements are a preferred option to manage uncertainty for new cancer medicines in most countries

26. Respondents to the 2023 OECD Policy Survey on Cancer Care Performance were asked what types of policies and/or approaches, if any, they use to address uncertainty when making coverage and/or pricing decisions for new cancer medicines/indications; see Figure 3.4. Almost all countries (24 out of 28 respondents) reported using financial MEAs. The exact implementation differs between countries and medicines within a country but could for instance include (confidential) rebates/discounts, price-volume agreements, or expenditure caps. 16 countries indicated that they use performance-based MEAs, which could include arrangements such as coverage with evidence development and payment-by-result. Eight countries reported using post-marketing studies to confirm evidence of clinical benefit. In Croatia, an additional approach for single-use cancer medicines (see also Box 3.1) exists, where the payment is made in several annual instalments over a certain number of years. For outpatient medicines in Austria, financial MEAs as well as other approaches are used, including conditional reimbursement leading to re-assessments/re-negotiations, and definition of restrictions of use to cover patients most likely to benefit from a new medicine with uncertain effectiveness.

Figure 3.4. Policies and/or approaches to address uncertainty in coverage and/or pricing decisions for new cancer medicines/indications

Based on responses from 28 countries (multiple options possible per country).



Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

27. Even though performance-based MEAs might be an attractive option to link payment to patient outcomes, they have several drawbacks. On the one hand, it might be complex to define and measure "performance" (outcomes) in various disease settings. On the other hand, there will be additional

administration to put a system in place that can monitor utilisation and outcomes and is able to link this information to financial settlements with the marketing authorisation holders. Countries may have constrained capabilities to establish such systems and/or integrate them within the existing structures (registries and electronic health records) and/or staff to run and maintain the systems. This creates an additional layer of inequalities between countries. In the 2023 OECD Policy Survey on Cancer Care Performance, Estonia noted that they concluded very few performance-based MEAs and use more financial MEAs, as they are easier to manage and usually also preferred by the pharmaceutical industry. A previous study of MEAs in Bulgaria, Croatia, Czechia, Hungary, Poland and Romania found that financial MEAs are used by all countries, whereas performance-based MEAs are scarce and only used to a limited extent by Hungary and Poland (Rotar et al., 2018[32]). In general, performance-based MEAs might be limited to cases with great uncertainty about clinical benefits and/or high anticipated budget impact, such as for the new drug class of CAR T-cell therapies, whereby data are able to be collected in order to address these uncertainties; see Box 3.1.

Box 3.1. Approaches to address uncertainties of CAR T-cell therapies

A new era for cancer treatment in the EU/EEA countries started in August 2018 with the approval of the first two CAR T-cell therapies (axicabtagene ciloleucel and tisagenlecleucel) by the EMA. These cell-based therapies are inherently different from previous types of cancer medicines. They only require a single intravenous administration of therapy instead of a repeated administration over several months or years. These therapies can also be expected to be curative (i.e., complete remission) for some patients. For example, the cure rate in patients with refractory large B-cell lymphoma is of around 40% (Bachy et al., 2022[33]). The unique features of the therapies represent new challenges and uncertainties in the assessment of clinical benefits and payment (Aballea et al., 2020[34]). Challenges include uncertainty about whether the curative effect really persists over time beyond the duration of the follow-up period in the clinical trials, the valuation of a curative therapy rather than a palliative therapy postponing death for a couple of months or years, and the temporal disconnection between the payment for the one-time treatment and the time during which the health economic benefits (i.e., value) are realised. The latter has been described as an "affordability barrier" (Michelsen et al., 2020[35]), where a medicine can be judged cost effective in the HTA process but not affordable with the current budget and payment modality based on "payment of the full price upon administration". The anticipated expanding utilisation of CAR T-cell therapies across multiple indications of haematologic cancers in the years until 2025 has been estimated to result in cumulative costs of around EUR 30 billion in six major European countries (France, Germany, Italy, the Netherlands, Spain, and the UK) between the years 2019 and 2029 (Heine et al., 2021[36]).

The first experiences with CAR T-cell therapies in France, Germany, Italy, Spain, and England showed that different payment models were used to address their unique features, uncertainties, and budget impact (Jørgensen, Hanna and Kefalas, 2020[37]). All payment models employed in these countries involved risk sharing between the healthcare payer and the pharmaceutical company. France and England chose "coverage with evidence development" to make reimbursement conditional on collecting additional data for future reassessments. In Germany, "outcomes-based rebates" were used where the pharmaceutical company grants rebates to the payer based on individual patient outcomes. In Italy and Spain, "outcomes-based staged payments" (annuity payments) were used to split the total payment for the therapy into two to three instalments that are linked to individual patient outcomes.

The availability of CAR T-cell therapies differs across the EU. The above-mentioned major countries in Western and Southern Europe were able to enable quicker access to patients after the regulatory approval in 2018. Patients in Eastern and Central European countries had to wait longer (Zamecnik, 2022[38]). In Czechia and Poland, the first patients were treated in late 2019 (Zamecnik, 2022[38]). In Romania, the first patient was treated in July 2022 (Van Kline, 2022[39]). The high costs but also logistical complexity in the production and administration of the therapies have been cited as reasons for these inequalities between countries (Zamecnik, 2022[38]). CAR T-cell therapies are only administered at specialized treatment centres. They require an extraction of cells from the patient, followed by shipment to the pharmaceutical manufacturers production facilities – of which there are few in Europe – and shipment back to the treatment centre for reinfusion (Vucinic et al., 2021[40]; Giorgioni et al., 2023[41]).

3.3 Availability and time to coverage of new cancer medicines

28. The availability and coverage of new medicines determines patient access. The definition of 'availability' may vary in different contexts and studies. It might refer to marketing authorisation, reimbursement/coverage approval, and/or first sales. In addition, the time to availability depends on both the starting point (e.g., the date of the application for regulatory approval or the date of the actual approval)

and the endpoint (e.g., the date of reimbursement/coverage or the date of first use in routine clinical practice). For EU countries, the Transparency Directive (Council Directive 89/105/EEC)[15] mandates maximum time limits for pricing and reimbursement decisions (90 days for pricing, 90 days for reimbursement or 180 days for combined pricing and reimbursement decisions) from the time a pharmaceutical company applies for pricing and reimbursement of a medicine to the country's competent authorities. However, if further information from the applying pharmaceutical company is needed, 'clock-stops' apply during the pricing and reimbursed negotiations. This may prolong the process beyond 180 calendar days (World Health Organization, 2018[20]).

Previous studies reported substantial differences in availability of new cancer medicines across European countries

29. Previous studies have generally revealed great differences across EU and OECD countries in terms of availability of cancer medicines and the time to availability. An OECD report from 2020 used a sample of 109 product/indication pairs across five major cancer types and assessed the reimbursement status at the end of 2019 (Chapman, Paris and Lopert, 2020[1]). 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 of pairs approved and covered (47% and 46% respectively). Of the 31 new product/indication pairs approved since 2014, the time from application for reimbursement until granting of reimbursement ranged from 4 months in Sweden to 27 months in Malta (Chapman, Paris and Lopert, 2020[1]). The European Federation of Pharmaceutical Industries and Associations (EFPIA) evaluates the reimbursement status of new cancer medicines on an annual basis. The latest numbers cover 46 cancer medicines with EMA approval in 2018-2021 and reimbursement status[16] at the beginning of January 2023 (Newton et al., 2023[42]). Their analysis revealed vast differences between EU countries, ranging from 45 out of 46 medicines (98%) being reimbursed in Germany to only one medicine (2%) being reimbursed in Malta. The mean time between EMA approval and reimbursement approval for medicines that had received a positive coverage decision was shortest in Germany with 102 days and longest in Romania with 991 days (Newton et al., 2023[42]).

30. The availability of distinct subgroups of cancer medicines has also been examined in various international studies. One such subgroup are 'essential cancer medicines', which are included in the World Health Organization's (WHO) Model List of Essential Medicines (EML). These are highly effective, but typically older medicines for which generic versions are available. An OECD report from 2020 found that the availability of essential cancer medicines used in the treatment of five major cancer types was fairly homogeneous among OECD/EU countries (Chapman, Paris and Lopert, 2020[1]). An earlier study of a broader set of cancer types also found that discrepancies among EU countries in the availability of cancer medicines on the WHO EML are small (Cherny et al., 2016[43]). However, both studies observed greater differences among the subgroup of newer cancer medicines that are not yet on the WHO EML (Chapman, Paris and Lopert, 2020[1]; Cherny et al., 2016[43]).

31. Partly in response to the growing number of new cancer medicines and their varying levels of clinical benefit, the European Society for Medical Oncology (ESMO), developed a value framework called Magnitude of Clinical Benefit Scale (MCBS)[17] in 2015 (Cherny et al., 2015[44]). The value framework offers a grading system of new indications of cancer medicines and their relative magnitude of clinical benefit

[15] Transparency Directive (Council Directive 89/105/EEC) https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A31989L0105, accessed August 2023.

[16] Inclusion of a centrally approved medicine on the public reimbursement list in a country

[17] See https://www.esmo.org/guidelines/esmo-mcbs/about-the-esmo-mcbs, accessed August 2023.

that can be anticipated from data derived from pivotal clinical trials or meta-analyses. ESMO proposed the MCBS to be used as a tool to support the process of prioritisation of access to cancer medicines by national health authorities when resources are constrained (Cherny et al., 2015[44]; Cherny et al., 2017[45]). Some previous studies have used the ESMO-MBCS to investigate whether the level of clinical benefit plays a role in both the likelihood to receive reimbursement approval as well as the time from marketing authorisation approval until reimbursement approval. An analysis of 124 cancer indications with EMA marketing authorisation in 2011-2020 and followed up until 2022 showed that a significantly greater proportion of indications with a substantial clinical benefit compared with a non-substantial benefit according to ESMO-MCBS was reimbursed in Czechia, Hungary, Poland, and Slovakia, yet there was no statistical difference in the time until reimbursement approval in any of the countries (Hofmarcher et al., 2023[46]). A similar analysis of 53 cancer indications applying for national reimbursement in Slovenia in the period 2008-2018 also failed to establish a statistically significant relationship between a substantial clinical benefit level and the time from EMA marketing authorisation until reimbursement (Janzic et al., 2019[47]).

There is a three-fold difference in the reimbursement of cancer medicines with a high clinical benefit in Europe

32. As part of the 2023 OECD Policy Survey on Cancer Care Performance, new information on the availability and time to coverage of new cancer medicines was collected for 25 EU/EEA/CH countries. A sample of all indications with the highest ESMO-MCBS score and with EMA marketing authorisation after 1st January 2016 with approvals in breast cancer and lung cancer was considered; see Annex A for a detailed description. Five different metrics were assessed for all indications; the application status for reimbursement on 1st April 2023; the reimbursement status on 1st April 2023; the time between the EMA marketing authorisation and the application by the pharmaceutical company for HTA / coverage in the public reimbursement list (Period 1 in Figure 1.1); the time between the reimbursement application and the reimbursement date (Period 2 in Figure 1.1); any restrictions/limitations in the reimbursed indication text compared to the text of the EMA approved indication.

33. The proportion of the indications in the sample reimbursed/covered on 1st April 2023 varied substantially across countries; see Figure 3.5. Germany reported that all indications were covered, followed by the Netherlands (92%) and Bulgaria and Sweden (both 85%).[18] Malta reimbursed no indications[19] and Cyprus and Latvia reported small proportions of indications covered (both 31%). However, the consideration of a specific indication for which multiple, similar alternatives are available showed a more favourable picture in terms of meeting patients' clinical needs. Table A A.3 in Annex A shows that across three specific indications in breast cancer and lung cancer with multiple alternative medicines available, only Cyprus (in one setting), Hungary (in one setting), and Malta (in all three settings) did not cover any of the available medicines.

[18] It should be noted that the mere inclusion of a medicine/indication in a positive reimbursement list does not mean that all eligible patients will have access in clinical practice. For instance, Figure 4.1 reveals that the use of immunotherapies in Bulgaria was among the lowest in the EU in 2018. Budget restrictions might inhibit the widespread use of a reimbursed medicine in practice in some countries.

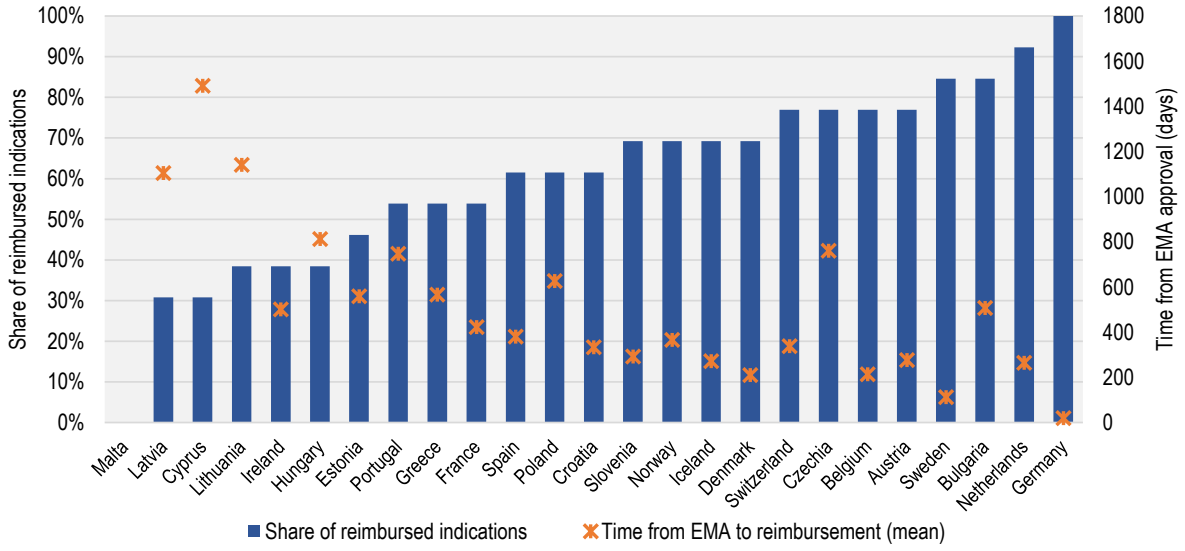
[19] In Malta, many indications were available through an early access scheme on a named-patient basis; see section 4.3.

Time from marketing authorisation until coverage decision ranges from less than 100 days in Germany and Sweden to over three years in Cyprus, Latvia, and Lithuania

34. The total time between EMA marketing authorisation[20] and reimbursement/coverage decision (Period 1+2) exhibited considerable variations; see Figure 3.5. It ranged from less than 100 days in Germany and Sweden to over 1100 days in Cyprus, Latvia, and Lithuania. This total time period is shaped by factors and processes that are in control of both the applying pharmaceutical company and the national authorities.

Figure 3.5. Share of selected indications of newer cancer medicines with public reimbursement/coverage and time from EMA marketing authorisation to reimbursement/coverage in the public reimbursement list

Based on responses from 25 countries.



Notes: 13 indications of ten cancer medicines used in the treatment of breast cancer and lung cancer with marketing authorisation by the EMA after 1st January 2016 and active authorisation on 26th March 2023 and with the highest clinical benefit according to the ESMO-MCBS scoring system (scores of A and 5) were included in the analysis. The public reimbursement/coverage status in the countries shows the situation on 1st April 2023. The mean of the time from EMA authorisation to public reimbursement/coverage was calculated based on the number of indications with valid reimbursement on 1st April 2023 and with valid information provided in the survey. In Malta, no indications were on the standard reimbursement list and no application dates were provided for specific indications, yet all indications were available on a named-patient basis. In Germany, a public reimbursement list does not exist, but rather reimbursement occurs with EMA authorisation and launch. For Switzerland, the time was calculated from the EMA approval date and not the national regulatory approval date.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

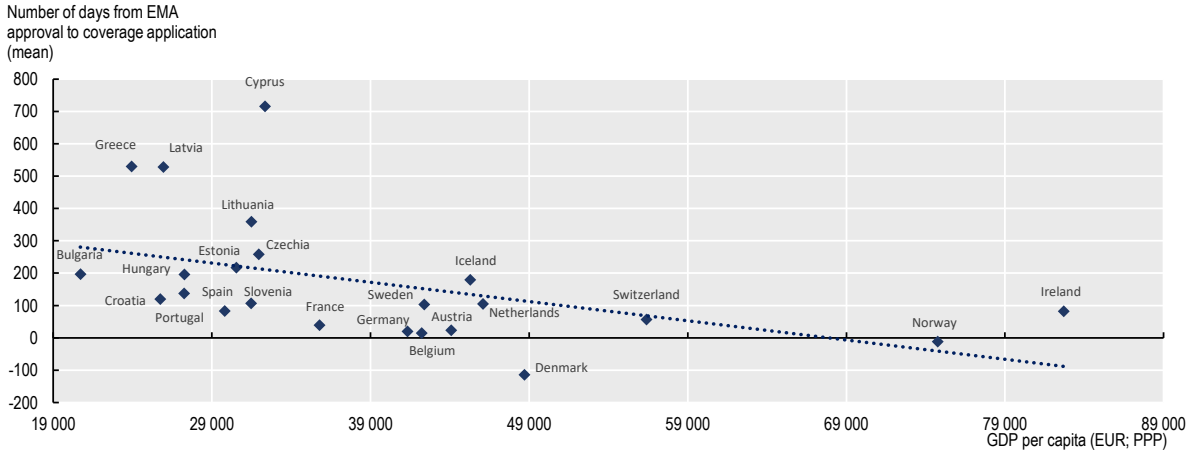
35. The period between EMA marketing authorisation and application for reimbursement by the pharmaceutical company (Period 1) is displayed in Figure 3.6. This period is often interpreted as a reflection of companies' launch strategies, which may in turn be influenced by national pharmaceutical policies. For example, in some countries, the application for coverage can be made prior to the receipt of marketing authorisation. Wide variations in the length of Period 1 were found among the responding

[20] In practice, the EMA CHMP only issues positive opinions, while the European Commission makes the final decision on marketing authorisation. However, for the sake of clarity in this report, we describe this process as "EMA marketing authorisation".

countries. Denmark and Norway had the shortest mean time between marketing authorisation and application for coverage (114 and 12 days before EMA authorisation, respectively), followed by Belgium (15 days after EMA authorisation). Latvia (528 days after EMA authorisation), Greece (530 days), and Cyprus (716 days) had the longest mean time. The announcement[21] from EFPIA member companies in 2022 to commit to file for pricing and reimbursement in all EU countries no later than 2 years from EMA marketing authorisation will likely have limited impact on cancer medicines. However, the negative correlation between the length of Period 1 and countries' GDP per capita (see Figure 3.6) is compatible with the idea that pharmaceutical companies may prioritize high-income markets where price expectations and willingness/ability to pay higher prices are greater.

Figure 3.6. Time from EMA marketing authorisation to application for reimbursement/coverage compared to countries' GDP per capita

Based on responses from 25 countries.



Notes: 13 indications of ten cancer medicines used in the treatment of breast cancer and lung cancer with marketing authorisation by the EMA after 1st January 2016 and active authorisation on 26th March 2023 and with the highest clinical benefit according to the ESMO-MCBS scoring system (scores of A and 5) were included in the analysis. The mean of the time from EMA authorisation to application by the pharmaceutical producer was calculated based on all applications (both reimbursed and non-reimbursed) submitted until 1st April 2023 and with valid information provided in the survey. Malta and Poland are not shown, because no application dates were provided for specific indications in Matla and application dates are confidential in Poland. For Switzerland, the time difference was calculated from the EMA approval date and not the national regulatory approval date. In Germany, there is no application for reimbursement, but reimbursement is automatically granted with authorization at time of launch.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

36. A company may decide not to apply for reimbursement for a certain medicine. The proportion of the indications in the sample applied for until 1st April 2023 varied substantially across countries as displayed in Figure 3.7. Eight countries – mostly countries with high GDP per capita – reported applications for all indications in the sample, whereas Malta, Hungary, and Cyprus had received applications for less than 40% of the indications. This indicates that there is a gap compared to the announced commitment[22]

21 See https://www.efpia.eu/news-events/the-efpia-view/efpia-news/new-proposals-from-the-research-based-industry-can-reduce-inequalities-in-patient-access-to-medicines/, accessed August 2023.

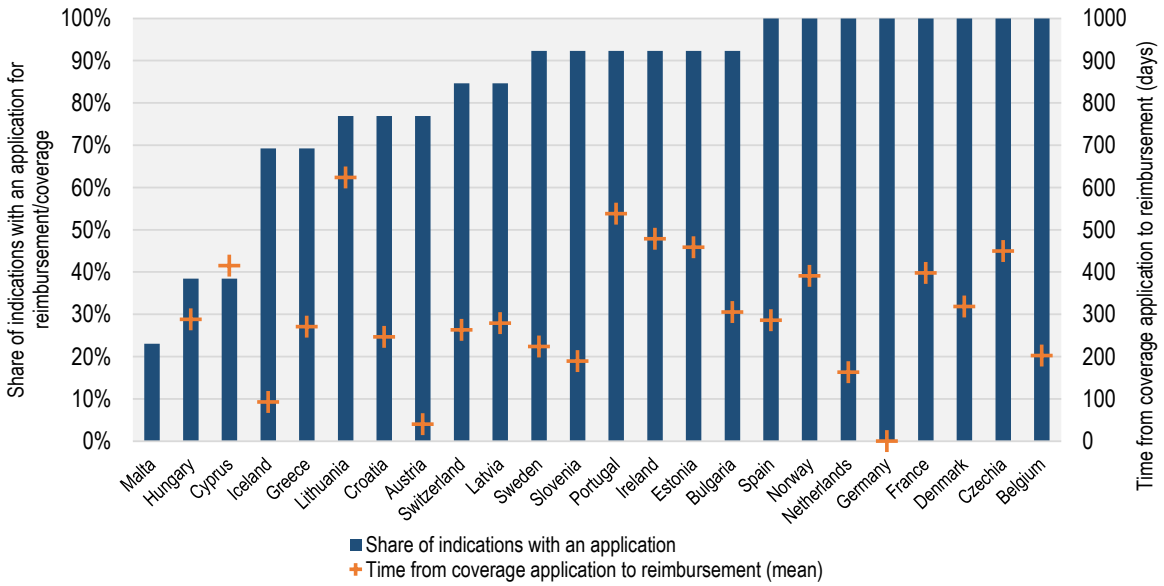
22 See https://www.efpia.eu/news-events/the-efpia-view/efpia-news/new-proposals-from-the-research-based-industry-can-reduce-inequalities-in-patient-access-to-medicines/, accessed August 2023.

from EFPIA member companies to file for pricing and reimbursement in all EU countries no later than 2 years from EMA marketing authorisation will likely have limited impact on cancer medicines.

37. The time between application for coverage by the pharmaceutical company and reimbursement decision (Period 2) is shown in Figure 3.7. This sequence is influenced by HTA processes and pricing mechanisms. In Germany, medicines are immediately reimbursed when an EMA marketing authorisation is issued and a product launched on the national market. Short mean periods of fewer than 180 days were also reported in Austria, Iceland, and the Netherlands. There might, however, be large differences between indications within a country, such as in the Netherlands where the period ranged between zero days for five indications and 518 days for another indication. The minimal time differences for certain indications in the Netherlands are because additional indications of already reimbursed medicines were automatically covered upon EMA authorisation due to special agreements (Lawlor et al., 2021[48]). Longer mean periods of more than 500 days were reported in Lithuania and Portugal. Observed delays are in most cases longer than the 180 days maximum defined in the Transparency Directive for EU countries' reimbursement and pricing procedures. However, in this working paper, the time measured includes "clock-stops" during which pharmaceutical companies are asked to provide additional information. Therefore, these delays cannot be interpreted as actual administrative processing time.

Figure 3.7. Share of selected indications of newer cancer medicines with an application for reimbursement/coverage and time from application to reimbursement/coverage in the public reimbursement list

Based on responses from 25 countries.



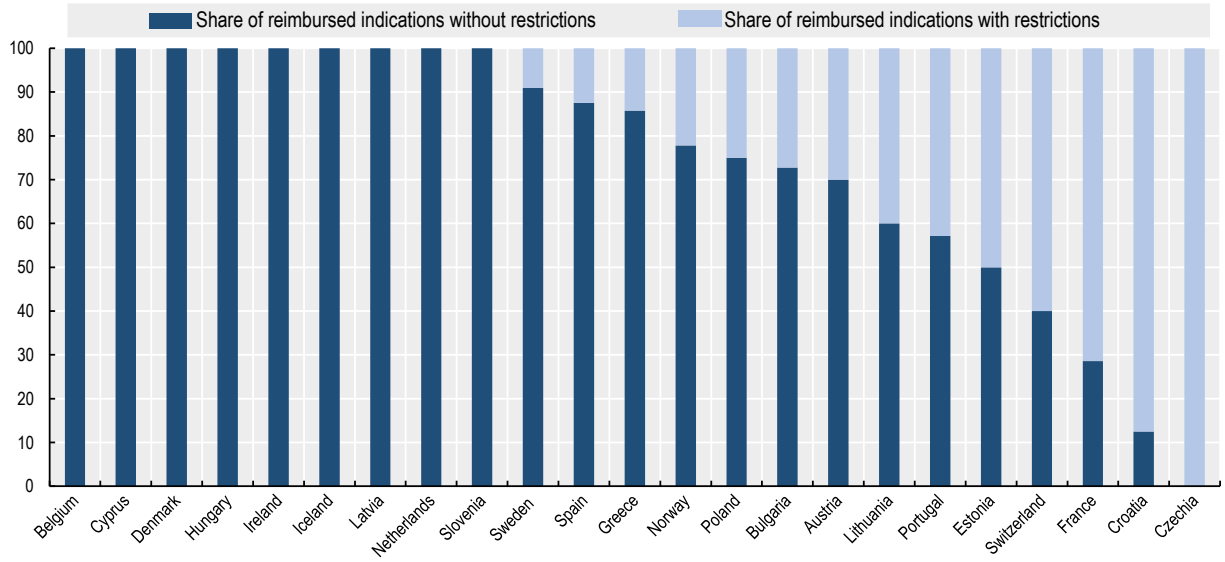
Notes: 13 indications of ten cancer medicines used in the treatment of breast cancer and lung cancer with marketing authorisation by the EMA after 1st January 2016 and active authorisation on 26th March 2023 and with the highest clinical benefit according to the ESMO-MCBS scoring system (scores of A and 5) were included in the analysis. The application status in the countries shows the situation on 1st April 2023. The mean of the time from coverage application by the pharmaceutical producer to public reimbursement/coverage was calculated based on the number of indications with valid reimbursement on 1st April 2023 and with valid information provided in the survey. In Malta, no application dates were provided for specific indications. In Germany, reimbursement occurs with EMA authorisation and launch. Poland is not shown because application status and dates are confidential.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

Some countries restrict the reimbursement of cancer medicines to smaller patient populations than those defined in the marketing authorisation

38. The reimbursement/coverage decision of a cancer medicine/indication might entail some restrictions to the eligible patient population. The national eligible patient population would thus be smaller than the patient population covered by the EMA authorisation. Examples of restrictions are requirements on the health status of patients, use in a particular line of therapy, treatment length, or cut-off value for gene expression. The purpose of these restrictions is to limit the uncertainty of clinical effectiveness in the patient group (e.g., by focusing on a subgroup of patients that demonstrated better response in the clinical trial) and/or to limit the budget impact (Hofmarcher et al., 2023[46]). Several countries did not report any restrictions to their reimbursed indications; see Figure 3.8. Estonia, Switzerland, France, and Croatia reported that more than half of all reimbursed indications have restrictions and Czechia reported that all indications had restrictions. These results mirror to some extent the findings of a broader analysis of 124 cancer indications with EMA marketing authorisation in 2011-2020 and followed up until 2022. This analysis found that all reimbursed indications in Czechia and Poland had restrictions, and in Hungary and Slovakia half and three-quarters of all reimbursed indications, respectively, had restrictions (Hofmarcher et al., 2023[46]).

Figure 3.8. Share of indications of newer cancer medicines with restrictions to the eligible patient population in their indication text in the public reimbursement list compared to the EMA-approved indication

Based on responses from 25 countries.



Notes: The underlying number of reimbursed indications varies from country to country and is shown in parentheses below the country labels. Restrictions in reimbursement/coverage were defined as "any restriction/limitation in the public reimbursement list on April 1, 2023 compared to the text of the approved indication by the EMA". These restrictions may limit the eligible patient population in various ways, such as through requirements on the health status of patients, the duration of treatment, or exclusion of subpopulations with certain molecular features of their tumours. Malta is not included as there were no indications on the standard reimbursement list.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

39. The workload for national decision-makers is increasing due to the growing number of cancer medicines and extensions of indications; see section 2.1. As reimbursement decisions are usually made at the indication level and not at the medicine level, the joint number of new cancer medicines and

indications reflects the true workload for national HTA and reimbursement bodies. In some countries, the increasing administrative workload could contribute to delays in the timelines of the HTA and ultimately the availability of new medicines/indications. In oncology, a development during the last few years has been the launch of medicines with many, consecutively introduced indications, in particular immune checkpoint inhibitors (Lawlor et al., 2021[48]). Some countries have sought solutions to address these medicines and find ways to quickly resolve the assessment of extensions in indications. Belgium and the Netherlands have applied so-called multi-year-multi-indication agreements, where future launches of new indications are automatically covered upon EMA approval without any prior HTA (Lawlor et al., 2021[48]). Even though this has helped to get immediate reimbursement/coverage (some of which is reflected in minimal differences between EMA approval and national approval in some indications covered in Figure 3.5), this approach is a departure of the principle of delivering evidence-based and cost-effective care. New indications generally have different effectiveness and cost implications for, e.g., biomarker testing, management of side effects, size of the target population, and other ancillary services, and call for a new assessment.

40. Future timelines of the assessment of new cancer medicines and extensions of their indications might see improvements in individual EU/EEA countries. The adoption of Regulation (EU) 2021/2282 on health technology assessment (HTAR) as part of the EU Pharmaceutical Strategy mandates joint clinical assessments and joint scientific consultations which will include the involvement of patients, clinical experts, and other relevant experts (European Commission, 2023[49]). This will apply to all new cancer medicines as of 12th January 2025. It is important to stress that the joint clinical assessment will not contain any analysis of costs, as they differ from country to country. National assessments of cost-effectiveness and budget impact thus will still be required in countries where this is part of the HTA process. In addition, it remains to be seen to which extent countries will rely on the joint clinical assessment or would still mandate their own assessment in complement, which would result in duplication of work both for national HTA bodies and pharmaceutical companies. Current voluntary cooperations in HTA between EU countries, such as Joint Nordic HTA-Bodies[23] (former FINOSE) in the Nordic countries and BeNeLuxA (Belgium, Netherlands, Luxembourg, Austria, and Ireland), might also see changes as a result of the HTAR; see a recent OECD report for more details on these cooperations (Chapman, Paris and Lopert, 2020[1]).

3.4 Reimbursement of companion diagnostics

In the past five years, half of new medicines targeting solid tumours were approved based on a biomarker

41. As described in section 2.1, the recent decade has seen the approval of a vast number of new molecularly targeted therapies and immunotherapies. The development of these medicines has been spurred by an increased biological understanding of the molecular drivers and features of tumours. For example, 15-20% of all breast cancers are characterised by the expression of human epidermal growth factor receptor 2 (HER2) and benefit from the administration of anti-HER2 targeted medicines (American Cancer Society, 2022[50]). Patients with non-small cell lung cancer benefit from medicines that target, for instance, the mutations in epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK) fusion, or ROS1 gene that are present in around 10-15%, 3-5%, and 1-2% of patients in Europe (Hofmarcher, Lindgren and Wilking, 2022[51]). The treatment with medicines is therefore increasingly becoming individualised and moving away from a one-size-fits all approach based on the tissue where the tumour originated.

[23] See: https://www.dmp.no/en/news/finose-becomes-joint-nordic-hta-bodies

42. The administration of targeted therapies requires prior testing for the presence of various targets (so-called predictive biomarker testing). The testing allows the identification of subgroups of patients that are expected to derive a clinical benefit from the therapies. A diagnostic test that is used to identify suitable patients for a specific medicine is called a “companion diagnostic”. The technologies used to perform biomarker testing underwent changes in the recent decade, moving away from analysing single biomarkers one at a time to parallel sequencing of biomarkers with next-generation sequencing (NGS) technology (Schwartzberg et al., 2017[52]; Tsimberidou et al., 2020[53]); see also Box 3.2.

Box 3.2. Reimbursement of biomarker testing with NGS technology

NGS is an advanced DNA sequencing technology that allows rapid and cost-effective sequencing of large amounts of genetic material (Mosele et al., 2020[54]). Depending on the exact NGS test, it can sequence dozens to thousands of genes simultaneously. Multi-gene testing with NGS has grown in importance over the last decade in certain cancer types. The prime example is advanced-stage non-small cell lung cancer (NSCLC), where an increasing number of medicines have received regulatory approval that target various mutations (more specifically, EGFR, ALK, ROS1, BRAF, NTRK, MET, RET, KRAS G12C, HER2), and where single biomarker testing for all of these mutations one at a time is no longer feasible (Hofmarcher, Malmberg and Lindgren, 2023[55]). In 2020, the European Society for Medical Oncology (ESMO) issued its first recommendation of routine use of NGS on tumour samples in advanced non-squamous NSCLC, prostate cancer, ovarian cancer, and cholangiocarcinoma (Mosele et al., 2020[54]).

Data from 2020 suggest that the adoption of NGS testing was likely still in its infancy in many countries in the EU (Normanno et al., 2022[56]). Table 3.2 shows that in most countries less than a quarter of tumours were analysed using NGS, whereas this was true for more than half of the tumour samples in Denmark and the Netherlands. For those patients that received an NGS test, its costs were covered by public reimbursement in 90-100% of cases in Cyprus, Denmark, Finland, Germany, Slovenia, Sweden, and the UK, while in most countries less than 75% of cases were covered. Several reasons for the low use and the lack of reimbursement of NGS tests in EU countries have been identified, including lack of diagnostic laboratory infrastructure with NGS testing capabilities, inefficient organisation of diagnostic testing, financial constraints, and failure to include NGS testing in local guidelines (Normanno et al., 2022[56]).

Table 3.2. Biomarker testing with NGS technology varies widely in the EU in 2020

Access dimension	Access level	Country
Uptake (% of all biopsies analysed with NGS technology)	0-24%	Belgium, Croatia, Czechia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Slovakia, Spain, UK
	25-49%	Austria, Cyprus, Portugal, Sweden
	50% or more	Denmark, Netherlands
Average proportion of all existing NGS tests that are publicly reimbursed	<75%	Bulgaria, Croatia, Czechia, Estonia, Greece, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia, Spain
	75-90%	Austria, Belgium, France, Ireland, Italy, Luxembourg, Netherlands, Portugal
	90% or more	Cyprus, Denmark, Finland, Germany, Slovenia, Sweden, UK

Notes: Uptake was calculated as the % of all biopsies analysed with NGS technology. Information for Bulgaria, Estonia, Luxembourg, Romania, and Slovenia only indicated an uptake of less than 50% but not an exact level, and information for Malta was missing. Reimbursement was calculated based on the average proportion of NGS tests reported to be covered by public reimbursement. Information on reimbursement for Malta was missing.

Source: (Normanno et al., 2022[56])

43. An analysis of all EMA approvals of new indications for solid tumours found that almost half (47%) of all approvals between 2015 and 2020 were based on a particular biomarker (Falcone et al., 2022[30]). In pricing and reimbursement decisions of new medicines/indications it is therefore vital to consider the presence of a companion diagnostic. Previous research has pointed out a paradoxical situation in which public healthcare payers may decide to reimburse a medicine but not its companion diagnostic (Mateo et al., 2022[57]). If patients cannot access the companion diagnostic, it will be difficult to access a targeted therapy even though it is reimbursed. In European countries with limited public reimbursement for companion diagnostics, patients, through out-of-pocket payments, or pharmaceutical manufacturers, through patient support programmes, may pay for the testing (Normanno et al., 2022[56]).

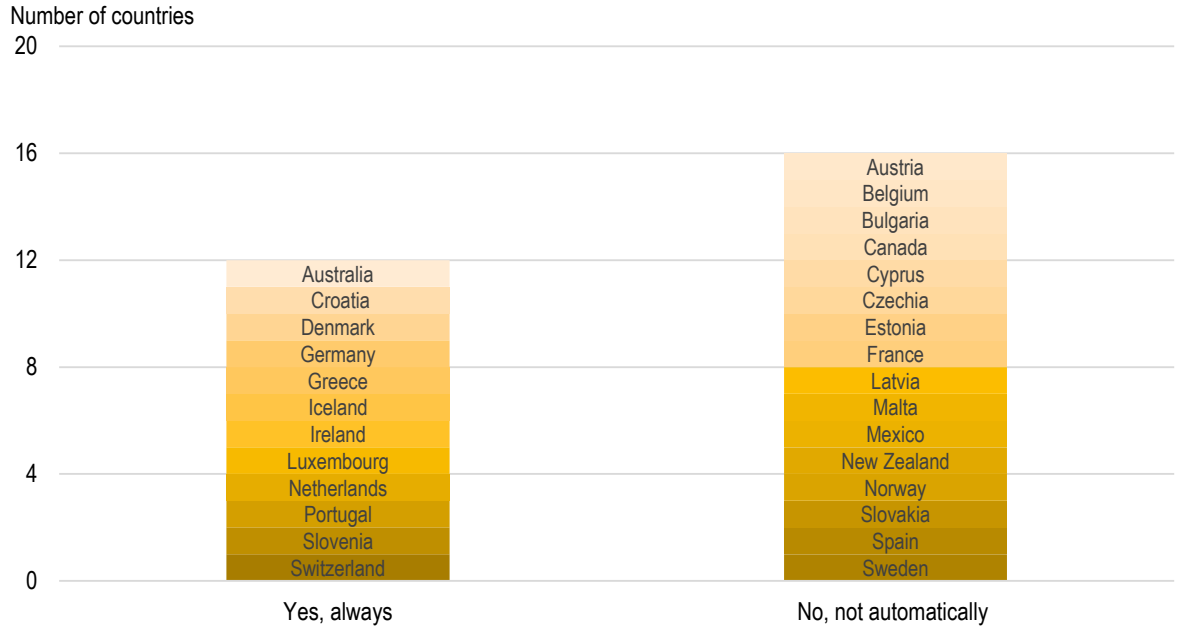
The reimbursement of a companion diagnostic is not coupled to the reimbursement of a matching medicine in a majority of countries

44. Respondents to the 2023 OECD Policy Survey on Cancer Care Performance were asked whether a companion diagnostic is automatically covered/reimbursed when a medicine/indication for which the marketing authorisation implies the required use of a companion diagnostic is covered/reimbursed; Figure 3.9. Fewer than half of countries stated an automatic link between the coverage/reimbursement decision for a medicine and its companion diagnostic. For instance, in Germany, the "Evaluation Committee" (Bewertungsausschuss) is required by law to adapt the outpatient sector reimbursement immediately and implement a reimbursement for medical services that are in line with the marketing authorisation of a medicine required for the use of the medicine. In Australia, in the case of "codependent technologies", the net clinical benefits, cost-effectiveness and financial implications of the joint use of the technologies are considered as part of the reimbursement decision, and the companion diagnostic and medicine/indication would become funded simultaneously. Yet, a majority of countries indicated that the coverage/reimbursement of companion diagnostics is not automatically coupled to the coverage of medicines.

45. In practice, the reimbursement of a companion diagnostic should occur in an integrated way with the reimbursement of the medicine. Additional costs of both the biomarker testing and the use of the new medicine need to be incorporated in the HTA process. The result of the HTA would then be either that both the companion diagnostic and the medicine are reimbursed or that neither are reimbursed. Unless the reimbursement is bundled together, the adoption of "personalised medicine" in clinical practice will be slowed down and potentially put a financial burden on patients in these countries.

Figure 3.9. Automatic coverage/reimbursement of the companion diagnostic upon coverage/reimbursement of a new cancer medicine/indication

Based on responses from 28 countries (one option possible per country).



Notes: In Malta, the HTA process is only applied to medicines but not to companion diagnostics. In Estonia, medicines and companion diagnostics are usually evaluated separately, but upon reimbursement of a medicine, the companion diagnostics will be made available. In Austria, a lump-sum payment is made in hospitals, which also covers the necessary companion diagnostics. In Sweden, the decisions regarding diagnostics are made directly by the healthcare regions, and if they are used on patients they are always reimbursed. In Canada, when a medicine is submitted for review to CADTH and/or INESSS, the diagnostic test that is required for the safe and effective use of the medicine is also evaluated as part of the medicine review process if the information is made available by the pharmaceutical manufacturer. As the coverage and reimbursement of companion diagnostics in Canada are typically made by provincial or territorial decision-makers, which have their own policies and procedures for funding decisions, a companion diagnostic is not automatically guaranteed when the medicine indication is covered. In New Zealand, companion diagnostics are not funded from the same budget as medicines, nor by the same agency, yet the availability, resource and financial impact of the companion diagnostic to the New Zealand health system is taken into consideration when making decisions on the assessment and funding of medicines by Pharmac. In Czechia, if a new medicine requires a new specific companion diagnostic or other testing (or generally, any other complementary care) that incurs additional costs, this must be included in the medicine's health-economic analysis of the HTA procedure, yet a brand-new diagnostic/device that is not covered under currently contracted healthcare, must be contracted separately by the healthcare provider and the health insurance funds.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

4 Uptake and utilisation of cancer medicines

46. The third, and most important, step for patient access to new cancer medicines is uptake or utilisation of medicines in clinical practice. Despite reimbursement by public healthcare providers, new medicines may take months or years until they are used on a broad scale in all treatment centres across a country and in all clinically eligible patients. University hospitals and comprehensive cancer centres may often be early adopters whereas other hospitals are typically slower. For new medicines to be used, clinical guidelines and protocols need to be adapted and medical staff needs to be updated and trained on how to use them safely and appropriately. Testing infrastructure might need to be established or extended, as many modern cancer medicines have a companion diagnostic (see section 3.4). High patient co-payments[24] on reimbursed cancer medicines can restrict the number of patients who can afford to be treated with new therapeutics. All these factors may contribute to inequalities in patient access to new medicines between and within countries.

47. Also, apart from standard coverage/reimbursement, there are other routes for patients to access to new medicines even before standard coverage/reimbursement. One route is through clinical trials. Another one is through early access systems. Patient access to older, established medicines is also important in the context of growing tensions on supply chains. Ensuring an efficient use of older medicines, especially for medicines for which generics and biosimilars are available, could help to stem the increasing financial burden of new cancer medicines.

4.1 Utilisation of oncology medicines in value and volumes

48. The reimbursement/coverage of medicines does not necessarily imply that patients will have access to them when seeking care. Countries with a high reimbursement/coverage (see section 3.3) might still be characterised by low utilisation in clinical practice. Cancer medicines utilisation can be measured in various ways, including via measuring costs (e.g., euros paid for medicines) and volume (e.g., milligrams of active substance of medicines administered).

[24] As prices of cancer medicines can be particularly high, cost-sharing requirements can substantially affect affordability for patients. Fixed co-payments are, in principle, more effective in providing financial protection than co-insurance, where contributions are set as a percentage of the cost of the medicine. A recent OECD report that researched co-payments for cancer medicines found that in many European OECD countries, patients can access inpatient and outpatient cancer medicines free of charge, especially if these are delivered by public providers (Chapman, Paris and Lopert, 2020[1]). In other countries, there are caps on user charges. These caps are defined in absolute or relative terms (e.g. a fixed amount or a proportion of household income). They typically represent less than 1-2% of the average wage in European countries but may exceed 9% in the United States (Chapman, Paris and Lopert, 2020[1]). It should also be noted that apart from co-payments on medicines, patients may face additional out-of-pocket payments when accessing medicines, in particular transportation costs to and from the hospital or the pharmacy.

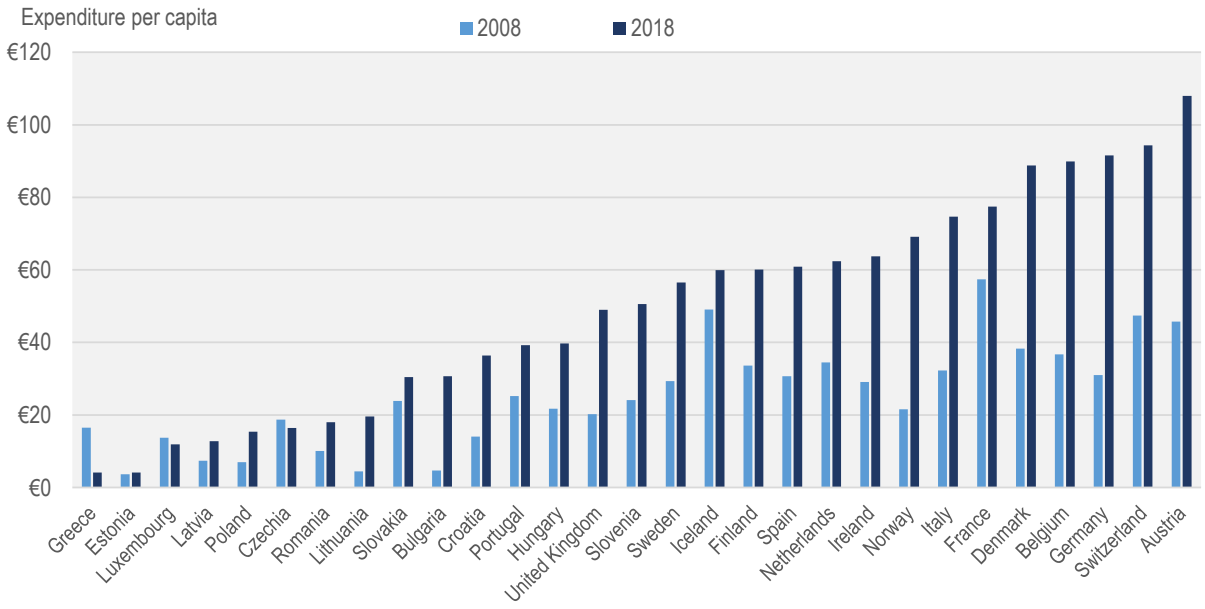
Expenditure on cancer medicines ranged from EUR 13 per capita in Latvia to EUR 108 capita in Austria

49. Comparable statistics on expenditure for cancer medicines are scarce, partly because net prices of medicines are not publicly available. Publicly available list prices of medicines may deviate from final net prices, because newer on-patent medicines are usually granted confidential rebates to public healthcare payers. These rebates may vary by medicine and also over time and between countries. Rebates in the range of up to 40-50% have been reported for cancer medicines in various European countries (Moye-Holz and Vogler, 2022[58]; van Harten et al., 2016[59]).

50. The direct costs – based on list prices and therefore overestimated – associated to the utilisation of cancer medicines are shown in Figure 4.1. Expenditure on all cancer medicines – among countries with complete data – ranged from EUR 13 per capita in Latvia to EUR 108 per capita in Austria in 2018. Countries in Western Europe tended to have the highest expenditure followed by countries in Northern and Southern Europe, whereas Eastern and Central European countries tended to spend the least. Total expenditure in the countries shown in Figure 4.1 more than doubled from EUR 12.9 billion to EUR 32.0 billion between 2008 and 2018, and per-capita expenditure went up from EUR 25 to EUR 61. This increase was observed to varying degrees by all countries with complete data. The inequalities in expenditure on cancer medicines thus did not become noticeably smaller between 2008 and in 2018.

51. (Hofmarcher et al., 2019[9]) suggest a long list of potential explanations for the surge in expenditure on cancer medicines between 2008 and 2018. One explanation is the increasing list prices of new medicines, which raise the costs per treatment. Evidence from the United States shows that list prices of branded cancer medicines have increased almost twice as strong as net prices (+59% vs. +35%, respectively) between 2007 and 2018 (Hernandez et al., 2020[60]), yet it is unclear to what extent the same pattern applies to European countries. Other explanations by (Hofmarcher et al., 2019[9]) relate to the increases in the utilisation/volume of medicines (see also Figure 3.3 in section 3.1) caused by the increasing number of cancer patients, the rising number of approved cancer medicines and indications, the multiplication of lines of therapy, greater use of combination therapies (i.e., older medicines not being replaced by newer medicines but used concomitantly), increasing use of cancer medicines in previously untreated patient groups (such as in the post-surgery adjuvant setting). All these factors can be expected to contribute to continued increases in expenditure on cancer medicines in the future.

Figure 4.1. Expenditure on cancer medicines per capita (in EUR, 2018 prices and exchange rates based on list prices, not adjusted for purchasing power parities), 2008 & 2018



Notes: Data for Estonia, Greece and Luxembourg only comprise retail sales and lack hospital sales in all years, and data for Czechia are incomplete in 2018. Cyprus and Malta are missing due to lack of data. The values shown for 2008 are from 2014 in Latvia, from 2009 in Romania, and from 2010 in Portugal. The expenditure data reflect sales data that are based on list prices, which often do not represent actual final sales prices because of confidential discounts/rebates to healthcare payers. Cancer medicines within the ATC groups L01 (antineoplastic agents), L02 (endocrine therapy), and L04 (immunosuppressants) were included.
Source: (Hofmarcher et al., 2019[9]) based on sales data from IQVIA.

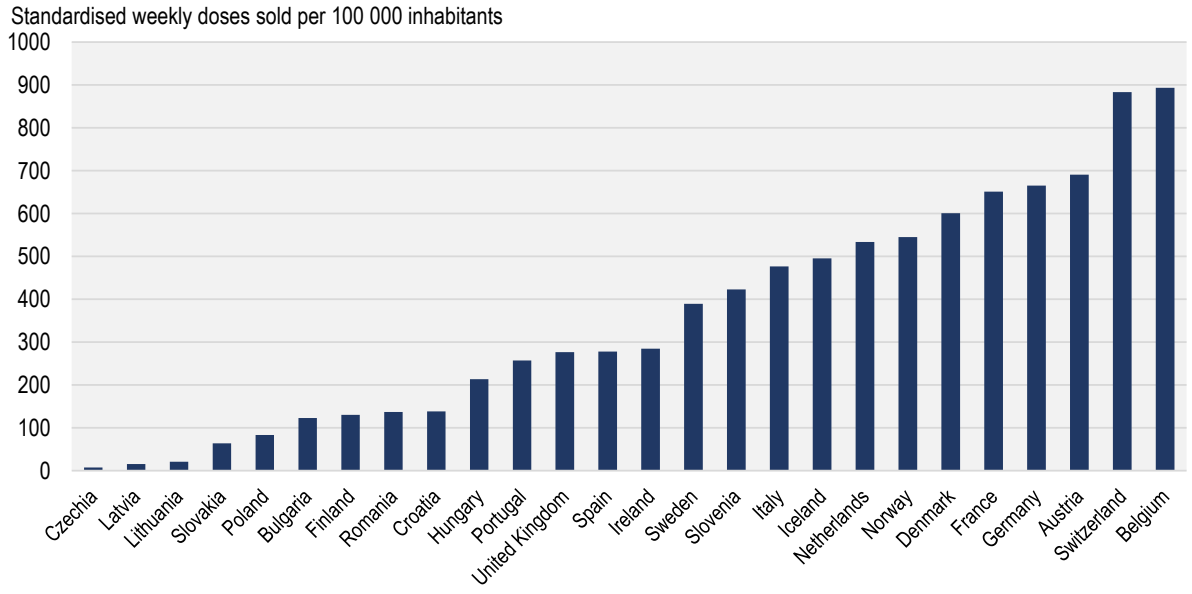
Eastern and Central European countries tend to have a lower utilisation of novel cancer medicines

52. Varying medicine prices, rebates, and exchange rates between countries complicate comparisons of the utilisation of cancer medicines in value. A comparison of the utilisation of medicines in volumes (milligrams) partly remedies these complications. The ideal measure would be to rely on defined daily dose (DDD), but DDDs are not established for all medicines with an ATC code[25]. Researchers have instead used approaches similar to DDD to standardise the utilisation of cancer medicines. The joint utilisation of four immunotherapies (approved by the EMA between 2011 and 2017) in volumes per 100 000 inhabitants in 2018 is shown in Figure 4.2. Among countries with complete data, Belgium and Switzerland had the highest utilisation rates, whereas Latvia and Lithuania recorded almost no utilisation at all. The pattern observed in Figure 4.2 mirrors to some extent the overall sales of cancer medicines in Figure 4.1, with mostly much lower utilisation in Eastern and Central European countries. Some part of the country differences in utilisation is explained by the fact that not all countries reimbursed/covered the four medicines and all their indications in 2018. An alternative approach to gauge utilisation based on treatment patterns across countries is shown in Box 4.1.

[25] Major drug groups without DDDs are topical products (most products in ATC group D), sera (ATC group J06), vaccines (ATC group J07), antineoplastic agents (ATC group L01), general and local anaesthetics (ATC group N01), ophthalmologicals and otologicals (most products in ATC group S), allergen extracts (ATC group V01) and contrast media (ATC group V08).

53. Apart from vast country differences in the utilisation of immunotherapies in volumes, (Hofmarcher et al., 2019[9]) showed that large differences are also apparent in cancer types that have seen the recent introduction of many new medicines, such as multiple myeloma and prostate cancer. In contrast, there are much smaller differences in the utilisation of certain older medicines, such as trastuzumab in breast cancer, yet even for these medicines there is a tendency of lower utilisation in Eastern and Central European countries compared to other countries in Europe.

Figure 4.2. Uptake of immunotherapies in volumes in 2018



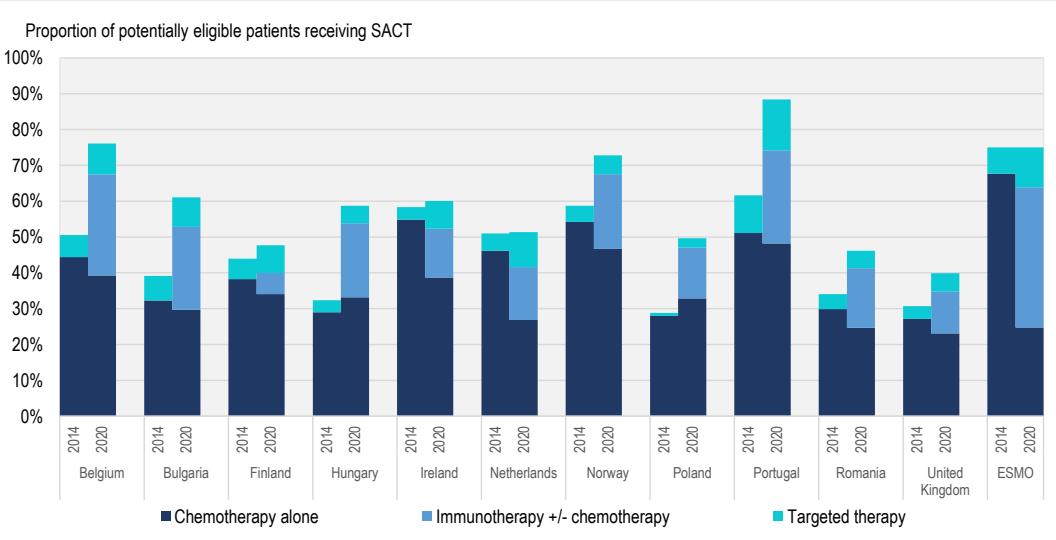
Notes: Data for Cyprus, Estonia, Greece, Luxembourg and Malta are not available. Data for Czechia are incomplete and hence underestimated. Four medicines, atezolizumab, ipilimumab, nivolumab, and pembrolizumab, are included. Standardised weekly doses were calculated based on data of milligrams of medicines sold. For each medicine, the total amount of milligrams sold was standardised with the weekly recommended dose in milligrams per patient, which yields the number of weekly doses sold. The weekly doses sold for all medicines were summed up and then divided by the number of inhabitants.
Source: (Hofmarcher et al., 2019[9]) based on sales data from IQVIA.

Box 4.1. Treatment patterns is another approach to comparing inequalities in access to cancer treatments

Measuring the utilisation of cancer medicines – in terms of costs or volumes – can only provide limited information on the quality of care that patients receive. To shed light on the quality of care, analyses of treatment patterns in different cancer types can be helpful. Ideally, real-world data from clinical registries should be used for this purpose. The data infrastructure and the level of detail contained in clinical registries on administered treatments might vary however and in some cases be completely absent. An analysis of treatment patterns would also be aided by a comparison with a benchmark that is derived from local clinical guidelines. Such a comparison could help to identify shortcomings in the care process in a country as a whole or at different institutions. In England and Wales, a so-called "National Lung Cancer Audit" has been conducted almost every year since 2007, which tracks various treatment patterns in lung cancer across the nations as a whole and also of individual NHS trusts (Royal College of Surgeons of England, 2023[61]).

A recent estimation of treatment patterns with cancer medicines in patients with advanced-stage non-small cell lung cancer (aNSCLC) across several European countries is shown in Figure 4.3. (Hofmarcher, Lindgren and Wilking, 2022[62]) estimated the proportion of potentially eligible patients with aNSCLC who receive treatment with cancer medicines (systemic anti-cancer therapy, SACT) and compared it to rates derived from clinical guidelines from ESMO. A comparison of the estimated SACT rates with the benchmark of a 75%-overall rate indicate that most countries seemed to treat a smaller proportion of patients with cancer medicines than what is recommended: the SACT rates differed considerably in both 2014 and 2020. They ranged from around 30% in Hungary, Poland, and the UK to almost 60% in Ireland, Norway, and Portugal in 2014. Until 2020, many countries had increased their SACT rates, ranging from around 40% in the UK to 75% or more in Belgium, Norway, and Portugal. In addition, the type of medicines administered deviated from the benchmark in nearly all countries in both 2014 and 2020. An underutilisation of both newer immunotherapy and targeted therapy in favour of older chemotherapy was evident. According to (Hofmarcher, Lindgren and Wilking, 2022[62]), the suboptimal treatment compared to the benchmark might be explained by factors such as the exclusion of patients with moderate health status from SACT, limited resources for diagnostic testing which is required for both immunotherapy and targeted therapy, long waiting times until reimbursement of newer medicines, and slow adoption of new medicines in clinical practice.

Figure 4.3. Rates of systemic anti-cancer therapy (SACT) for advanced non-small cell lung cancer (aNSCLC)



Notes: "Chemotherapy alone" = as monotherapy or platinum-based chemotherapy possibly also including combination with angiogenesis inhibitors; "Immunotherapy + /-chemotherapy" = as monotherapy or in combination with platinum-based chemotherapy and possibly also

including angiogenesis inhibitors; "Targeted therapy" = as monotherapy or in combination with angiogenesis inhibitors. The benchmark draws on ESMO treatment guidelines in its versions from 2014 and 2020, as well as on the year of approval of ESMO-recommended cancer medicines by the EMA. For the overall benchmark, 25% of both newly diagnosed patients at advanced stage and recurrent patients from earlier stages were assumed to receive best supportive care as first-line therapy due to ECOG PS 3–4, resulting in an optimal treatment rate of 75%. The composition of the types of therapy in the benchmark is based on the prevalence of relevant mutations seen in European patients as well as on assumptions on progression rates from first-line therapy to second-line and third-line therapy. SACT rates for 2020 are less robust due to the COVID-pandemic.

Source: (Hofmarcher, Lindgren and Wilking, 2022[62]).

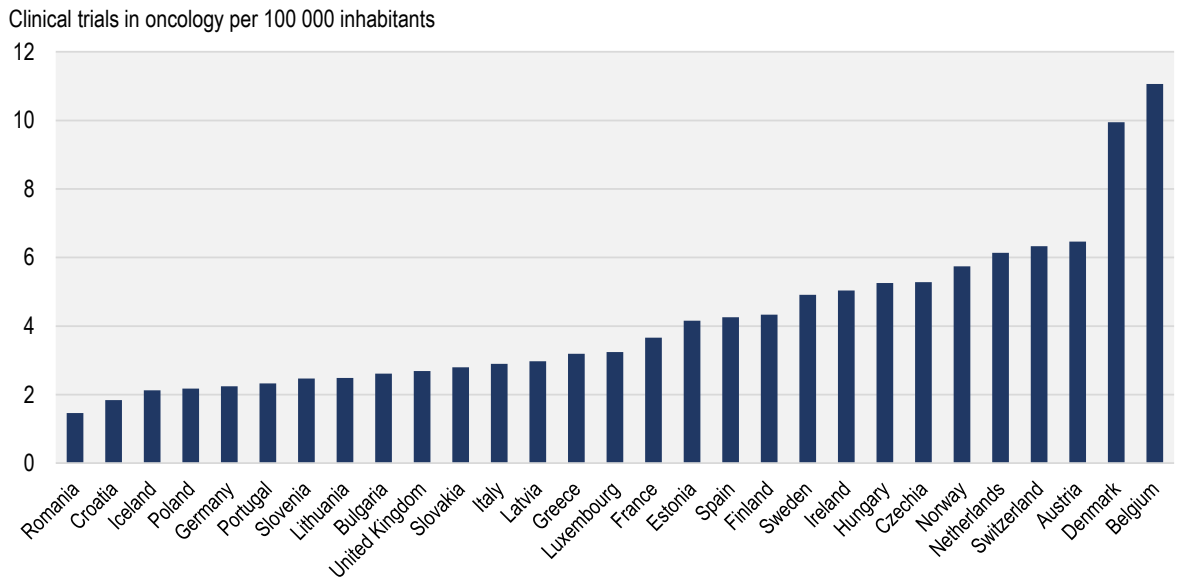
4.2 Access to clinical trials

54. Clinical research is critical for developing new medicines to treat cancer. Prior to regulatory approval and reimbursement/coverage decision, new medicines are extensively tested in clinical trials; see Figure 1.1 and Box 2.1. Participation in clinical trials offers a route to early access to new medicines for patients. However, access to clinical trials might be uneven across European countries and within countries, as they are mostly provided in certain institutions, such as university hospitals, making it difficult for patients treated in smaller hospitals in rural areas to access them.

The availability of clinical trials in oncology ranges from fewer than 2 trials to more than 10 trials per 100,000 inhabitants across the EU

55. Little systematic information on the geographical distribution and access level to clinical trials in oncology exists in Europe. An analysis by (Carneiro et al., 2020[63]) investigated the presence of phase I-III trials between 2009 and 2019 across European countries. In absolute numbers, most trials were conducted in France (with 2,344 trials), followed by Spain, Germany, the UK, and Italy (all between 1,745 and 1,994 trials). The number of trials per 100,000 inhabitants was lowest in Romania and Croatia with fewer than 2 trials per 100,000 inhabitants and highest in Denmark and Belgium with 10 or more trials per 100,000 inhabitants (Figure 4.4). (Carneiro et al., 2020[63]) also found that the number of clinical trials in oncology increased between 2010 and 2018 in Europe overall, being more pronounced in early phase trials. Yet some countries, especially in Eastern and Central Europe, saw a decline in the number of trials over time, which might reinforce already existing disparities to access oncology clinical trials in Europe. Inequalities in access to oncology clinical trials are also vastly documented in countries like the United States, see Box 4.2.

Figure 4.4. Clinical trials in oncology per 100 000 population in 2009–2019



Notes: Data include interventional phase I, phase I/II, phase II, phase II/III, and phase III trials in oncology (neoplasms) in adult patients starting between 1st June 2009 to 1st June 2019 and registered in the ClinicalTrials.gov database.
Source: Unpublished data from (Carneiro et al., 2020[63]).

Box 4.2. Inequalities in access to oncology clinical trials are well documented in the United States

In the United States, disparities in access to oncology clinical trials exist along several dimensions, such as race/ethnicity, income, and geography.

According to the FDA Drug Trials Snapshot for 2015-19, over 70% of clinical trial participants in the United States were White, although racial and ethnic minorities comprised almost 40% of the general population (Peters et al., 2023[64]). In addition, a retrospective analysis of 50 411 patients diagnosed between 2017 and 2022 from 280 cancer clinics, found that participation in clinical trials was lower among Black (4.2%) and Latino (4.4%) patients compared with White patients (7.2%) (Pittell et al., 2023[65]).

Other research has shown that counties in the United States with greater social vulnerability (as measured by the Centers for Disease Control and Prevention Social Vulnerability Index) were less likely to have a cancer clinical trial available in the period 2007 to 2022, ranging from around 50% in the quintile of the most vulnerable counties to almost 70% in the quintile of the least vulnerable counties (Sekar, Herrel and Stensland, 2024[66]). Moreover, the least vulnerable counties had around three times as many clinical trials per 100 000 inhabitants compared with the most vulnerable counties.

An analysis of 701 clinical trials in the United States found geographic disparities in the distance to clinical trial sites for patients diagnosed with common advanced-stage cancers (Swenson et al., 2024[67]). Although a majority of the population lives within 30 miles of a clinical trial site, the percentage varied based on the cancer type (breast, 81.8%; colon, 62.9%; lung, 82.0%; pancreatic, 65.7%; and prostate, 81.5%).

4.3 Early access systems

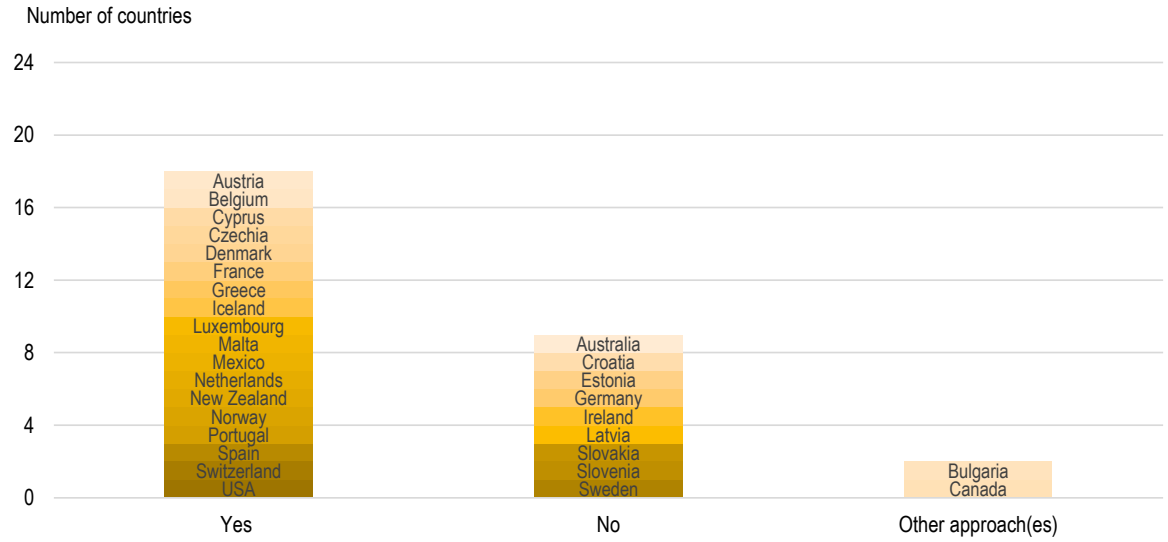
56. Early access schemes or programmes make a medicine available to a patient prior to marketing authorisation and/or the publicly funded coverage/reimbursement decision in a country. These schemes may generally apply to promising medicines used in severe conditions with high unmet need and no therapeutic alternatives; see a recent OECD report for a more detailed general description (OECD, n.d.[68]).

Many countries use early access systems to improve access to novel cancer medicines

57. Respondents to the 2023 OECD Policy Survey on Cancer Care Performance were asked whether such schemes or programmes currently exist, disregarding compassionate use programmes[26] regulated by Article 83 of Regulation (EC) No 726/2004 in EU countries. Early access schemes for cancer medicines exist in 18 out of 29 responding countries (Figure 4.5). Nine countries did not report to have them. One of the latter countries is Germany, where there is in general no real need for them, because all medicines authorised by the EMA are immediately available and reimbursed, unless the pharmaceutical company does not place them on the market. In addition, in Bulgaria, if the treatment of a relevant disease lacks an appropriate medicine because it has no market authorisation (but has one in another EU member state) or has a valid one but is not sold in the Bulgarian market, an individual patient may apply to receive this medicine. Canada has an early access mechanism to provide patients with access to new medicines before they are approved for general use by Health Canada. The Special Access Program (SAP) allows healthcare practitioners to request access to medicines that are not yet authorised for sale in Canada but are needed to treat patients with serious or life-threatening conditions. The SAP allows patients to receive access to medicines when conventional therapies have failed, are unsuitable, or are unavailable.

Figure 4.5. Presence of early access schemes or programmes for cancer medicines

Based on responses from 29 countries (one option possible per country).



Notes: Countries were asked to disregard 'compassionate use programmes' (regulated by Article 83 of Regulation (EC) No 726/2004) in their responses. In Estonia, a named-patient reimbursement system exists, but it is used for unlicensed medicines or for use in an off-label/not reimbursed indication rather than as a method to provide early access.

[26] See https://www.ema.europa.eu/en/human-regulatory/research-development/compassionate-use, accessed July 2023.

Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

Most countries rely on named-patient early access schemes

58. Two basic types of early access schemes exist. One type are population-based schemes, which extend to the entire target population within the scope of a medicine. Only a handful of countries indicated the presence of such schemes for cancer medicines in the 2023 OECD Policy Survey on Cancer Care Performance; see Table 4.1.

59. The more common type of early access schemes are named-patient schemes. In these schemes, patient access to a medicine is granted in response to a request by a patient and/or the treating physician on behalf of a specific patient on a case-by-case basis. The request may have to go through a rigorous review process and strict criteria may be applied, such as "the medicine being the only therapeutical option for the particular patient" in the case of Czechia. Both types of early access schemes may grant access to a medicine before marketing authorisation and/or after marketing authorisation. According to the survey responses, both scenarios of schemes granting access pre or post marketing authorisation are about equally common; see Table 4.1. Early access schemes are either funded by pharmaceutical companies (i.e., industry-sponsored) or third-party payers (i.e., government or insurer sponsored). Both funding arrangements exist in about equally many countries and some countries indicated the presence of both arrangements; see Table 4.1.

Table 4.1. Features of early access schemes or programmes most frequently used

Based on responses from countries which answered 'Yes' in Figure 4.5 (multiple options possible per country).

Type	Timing		Funding arrangement	
	Before marketing authorisation	**After marketing authorisation**	**Industry-sponsored**	**Government or insurer sponsored**
Population-based	Belgium, Denmark, France, Portugal, USA	Belgium, France, Mexico, New Zealand, Portugal	Mexico, Denmark, Portugal, USA	Belgium, France, New Zealand, Portugal
Named-patient basis	Austria, Belgium, Czechia, Denmark, Iceland, Greece, Luxembourg, Netherlands, New Zealand, Switzerland, Slovenia, USA	Belgium, Czechia, Cyprus, Greece, Luxembourg, Malta, New Zealand, Norway, Slovenia, Spain, Switzerland	Austria, Denmark, Greece, Luxembourg, Netherlands, Slovenia, Spain, Switzerland, USA	Belgium, Czechia, Cyprus, Greece, Luxembourg, Malta, New Zealand, Norway, Slovenia, Spain

Notes: Not all countries responding 'Yes' in Figure 4.5 provided answers. In Czechia, the response only refers to the public (insurance companies)-funded approach, whereas other industry-sponsored funding approaches cannot be excluded.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

Only a small proportion of clinically eligible patients typically benefits from early access schemes for a specific cancer medicine

60. In countries with early access schemes, these are never used for all new cancer medicines and not all clinically eligible patients may benefit from them. Respondents in the 2023 OECD Policy Survey on

Cancer Care Performance were asked to indicate how many clinically eligible patients usually benefit from early access schemes for a specific medicine/indication (Table 4.2). A majority of countries stated that fewer than 10% of the eligible patients benefit. Only in Switzerland and Mexico, more than half of the clinically eligible patient population usually benefits from the schemes. Small patient populations benefiting from early access schemes have previously also been documented in France. An analysis of the now abolished and replaced French temporary authorisation programme (ATU) found that in the 13 years between 1st January 2007 and 31st December 2019 only 16,927 French cancer patients were able to benefit from cancer medicines within the ATU (Jacquet et al., 2021[16]). This equalled on average 1,302 patients per year, which is only a very small fraction of the around 382,000 newly diagnosed cancer cases in France in 2018 alone (Jacquet et al., 2021[16]). Despite the advantage of providing early access to some patients, early access schemes seem to create within-country inequalities between cancer patients.

Table 4.2. Scope of early access schemes or programmes

Based on responses from countries which answered 'Yes' in Figure 4.5 (multiple options possible per country).

Scope	Fewer than 10%	Fewer than 50%	More than 50%
Proportion of clinically eligible patients who usually benefit from an early access scheme or programme for a given medicine/indication	Belgium, Denmark, Iceland, Luxembourg, Slovenia, Spain	Czechia, Greece, Malta, Portugal	Mexico, Switzerland

Notes: Not all countries responding 'Yes' in Figure 4.5 provided answers.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

4.4 Availability of generics and biosimilars

61. Upon patent expiration of medicines (and/or loss of market exclusivity), generics and biosimilars can enter the market and start to compete with the reference medicine (also called originator product). Competition between the producer of the originator product and the producer(s) of generics and biosimilars is expected to result in lower prices and cost savings. Rising prices of newer cancer medicines and the increasing budgetary pressure (see section 3.1) have put a spotlight on the financial sustainability of cancer care systems. Encouraging the entry and use of generics and biosimilars when the originator product has gone off patent is becoming increasingly important in oncology (Godman et al., 2019[69]). By achieving savings from the use of generics and biosimilars, this can redirect financial resources, helping to pay for newer medicines and increase financial sustainability.

Recent and upcoming patent expirations in oncology are expected to alleviate part of the financial pressure

62. The steep increase in the number of new cancer medicines in the past two decades (see section 2.2) means that the opportunities to achieve savings through the use of generics and biosimilars will rise in the coming years and decade (Godman et al., 2019[69]). In particular, biosimilars of three blockbuster medicines – bevacizumab, rituximab, trastuzumab – have in recent years received regulatory approval by the EMA (see section 2.2). These products were the three top-selling cancer medicines in 2012 and 2015, and they still accounted for 15% of total sales in Europe in 2018. Biosimilars for other medicines, for instance for cetuximab, pertuzumab, or denosumab are in development (Busse and Lüftner, 2019[70]; Bachu et al., 2022[71]). The development of biosimilars for the two top-selling immune checkpoint inhibitors

– nivolumab and pembrolizumab both approved by the EMA in 2015 – will be especially important as they are used across more than a dozen of cancer types and in different disease stages and have a significant budget impact on health systems. Patent expiry or loss of exclusivity is expected to occur around the year 2028 for both products.[27]

Yet, there are still important country differences in the proportion of biosimilars being reimbursed

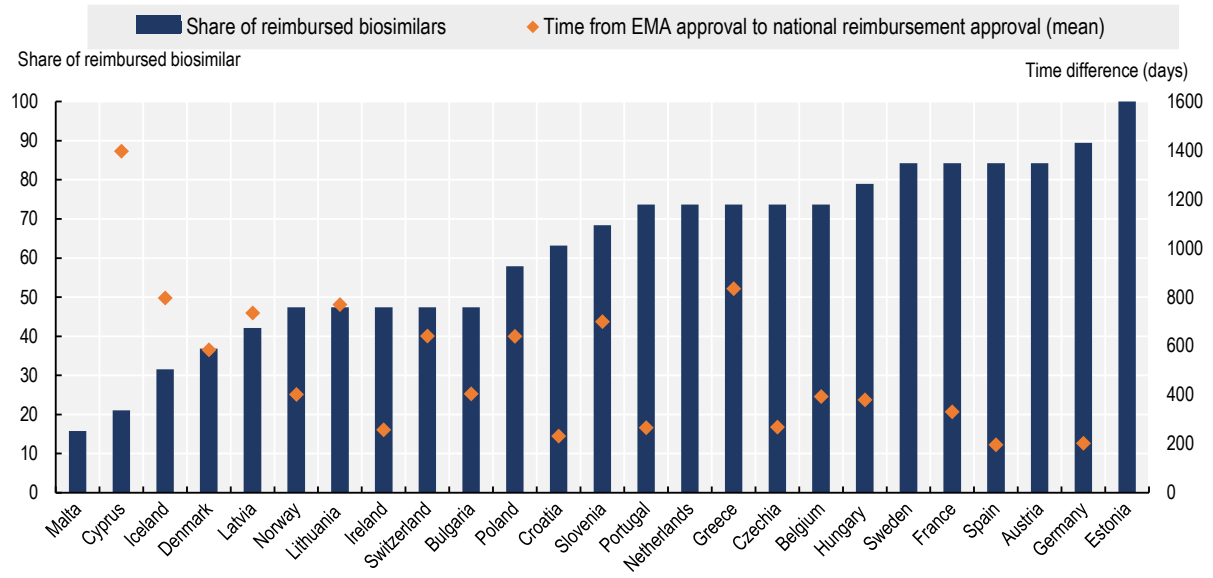
63. To describe the current environment for the utilisation of biosimilars in oncology, respondents to the 2023 OECD Policy Survey on Cancer Care Performance from 25 EU/EEA/CH countries were asked about the availability and time to availability of 19 biosimilars that have been approved by the EMA for bevacizumab, rituximab, and trastuzumab; see Annex B for a detailed description. The survey results revealed great differences in the share of biosimilars with public reimbursement/coverage across the responding countries; see Figure 4.6. In Estonia, all biosimilars are used in hospitals and which particular brand is used in a hospital depends on tender results. In Malta, only three biosimilars (16%), one for each medicine, are available on the Government Formulary following a competitive procurement procedure. All countries with the exception of Cyprus had at least one biosimilar reimbursed for each of the three medicines. Cyprus did not use to have a biosimilar for the medicine bevacizumab, but this changed as of May 2023.

64. The mean time from EMA approval to public reimbursement/coverage also exhibited great variations between countries, ranging from around 200 days in Germany and Spain to between 700 and 835 days in Greece, Iceland, Latvia, Lithuania, and Slovenia and almost 1400 days in Cyprus; see Figure 4.6. Countries with a higher share of publicly reimbursed/covered biosimilars also tended to have shorter time differences until public reimbursement/coverage.

[27] See https://www.fiercepharma.com/special-report/top-15-blockbuster-patent-expirations-coming-decade and https://scrip.pharmaintelligence.informa.com/SC146175/The-Next-Big-Patent-Cliff-Is-Coming-And-Time-Is-Running-Out-To-Pad-The-Fall, accessed August 2023.

Figure 4.6. Share of biosimilars for cancer medicines with public reimbursement/coverage and time between EMA approval and reimbursement/coverage

Based on responses from 25 countries.



Notes: 19 biosimilars of three cancer medicines (bevacizumab, rituximab, trastuzumab) with active marketing authorisation by the EMA as of 26th March 2023 were included in the analysis. The public reimbursement/coverage status in the countries shows the situation on 1st April 2023. The mean of the time difference was calculated based on the number of biosimilars with valid reimbursement on 1st April 2023. For Austria, Estonia, Malta, the Netherlands, and Sweden, no data on reimbursement dates was provided. In Estonia, all biosimilars are used in hospitals and which particular brand is used in a hospital depends on tender results. In Sweden, the biosimilars of these medicines are regionally procured and numbers here reflect only those on the market in any region. In Austria, all three medicines/substances are listed in the national 'Leistungskatalog' and biosimilars with an EMA approval can be reimbursed; the numbers here reflect only those biosimilars on the market. In Ireland, the number of reimbursed biosimilars in certain hospitals could be underestimated, because hospitals can negotiate arrangements with individual manufacturers. For Switzerland, the time difference was calculated from the EMA approval date and not the national regulatory approval date.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

4.5 Pricing and substitution policies for generics and biosimilars

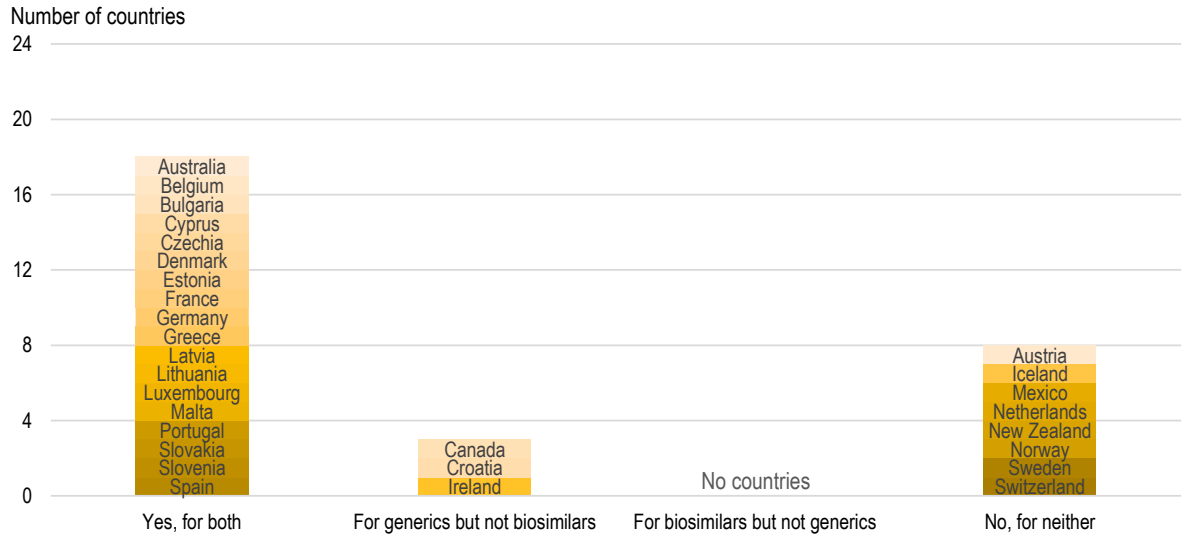
65. Different policies exist to stimulate the utilisation of generics and biosimilars when they become available in clinical practice (Vogler et al., 2021[72]). This includes pricing policies of various forms, such as internal reference pricing, where medicines with identical or similar active substances are clustered into groups and a common price is defined for all medicines within those groups. Prices of generics/biosimilars might also be linked to the price of the originator product through a system where mandatory discounts apply to generics/biosimilars which might increase with the number of generics/biosimilars entering the market. The price of the originator product might also face a mandatory price cut upon market entry of generics/biosimilars (Godman et al., 2019[69]; Moorkens et al., 2017[73]).

Reference price systems for both generics and biosimilars are in place in a majority of countries

66. Respondents to the 2023 OECD Policy Survey on Cancer Care Performance were asked whether a reference price system (RPS)[28] is in place specifically for generics and biosimilars used in oncology; see Figure 4.7. 18 out of 28 countries have such a system for both generics and biosimilars. In Australia, Estonia, and France, generic and biosimilar medicines are priced with reference to the originator product. Canada, Croatia, and Ireland are the only countries with an RPS for generics but not for biosimilars. In Canada, the pan-Canadian Pharmaceutical Alliance (pCPA) has developed the pan-Canadian Generic Tiered Pricing Framework which is comprised of three pricing tiers and applies to any generic product, where the current or previously available brand reference product was eligible for reimbursement by any participating pCPA jurisdiction. Biosimilars are not included in the Generic Tiered Pricing Framework and instead each biosimilar manufacturer for both oncology and non-oncology biosimilars undergoes national negotiation through the pCPA. 8 countries do not rely on an RPS for generics and biosimilars. Austria has no RPS in which identical or similar medicines are clustered and reimbursed at the same amount; instead prices of generics and biosimilars included in the outpatient reimbursement list are set in relation to the prices of the originator products. In New Zealand, a competitive procurement process is used to identify a preferred supplier that generally is awarded a 95% share of the reimbursed market for 3 years.

Figure 4.7. Reference price system for generics and biosimilars used in oncology

Based on responses from 28 countries (one option possible per country).



Notes: Some countries that have indicated the existence of a reference price system might not rely on a system of internal reference pricing with a common price for identical/similar medicines, but rather a system where the prices of generics/biosimilars are linked to the originator product.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

[28] Reference price system is a reimbursement policy in which identical medicines (ATC 5 level) or similar medicines (ATC 4 level or other groups) are clustered (reference group). The public payer funds a maximum amount (the reference price), while the patient must pay the difference between the reference price and the pharmacy retail price of the medicine (if any), in addition to any co-payments (such as prescription fees or percentage co-payment rates).

Generics and biosimilars can lead to substantial price reductions

67. Price drops after the introduction of generics and biosimilars might be considerable. The relative price difference between the originator product and a generic might be larger than that of a biosimilar due to higher research and development for biosimilars (Blackstone and Joseph, 2013[2]; Generics and Biosimilars Initiative, 2022[74]). Summarised research in another OECD report has indicated relative price differences of up to 80% for generics and 15-30% for biosimilars (Chapman, Paris and Lopert, 2020[1]). An analysis of biosimilars in oncology in Europe indicated reductions in list prices of 12% (Troein, Newton and Scott, 2020[75]). Price reductions in net prices of the originator product may also occur but are more difficult to ascertain due to the confidentiality of such information, but rebates of up to 90% of the list price have been reported (including of biologics used outside oncology) (Troein et al., 2022[76]). (Godman et al., 2019[69]) looked at nine generic oral cancer medicines included in the WHO EML across 25 EU countries. TheUSy observed that differences between the prices of originator products and generics varied widely across countries. For example, for imatinib in Norway, the Netherlands, Sweden, and Poland the differences were 40%, 42%, 96%, and 99%, respectively (Godman et al., 2019[69]). In the United States., biosimilars generate substantial savings despite having a more limited uptake compared to other OECD countries (see Box 4.3). Despite the savings that such price reductions can enable, there is also a risk of medicine shortages (at least temporarily) if the prices become too low and manufacturers pull their products from the market, mostly in the case of generics (Godman et al., 2019[69]).

Box 4.3. Limited adoption of biosimilars in the United States reduces potential savings

The potential to achieve savings through the use of biosimilars is well recognised in the United States. Early estimations showed that biosimilars could reduce direct spending on biologics by USD 54 billion from 2017 to 2026 or about 3% of total estimated biologic spending over the same period (Mulcahy, Hlavka and Case, 2018[77]). A more recent analysis demonstrated that biosimilar substitution in oncology reduced mean total cost of care (TCOC) per care episode by USD 1 193, equivalent to 2.4% of the mean TCOC (Yang et al., 2024[78]). Another study showed that savings per dose of trastuzumab and bevacizumab amounted to USD 261 and USD 366, respectively (Abdelmeseh et al., 2023[79]).

Nevertheless, the approval and uptake of biosimilars has been slower in the United States compared to in the EU/EEA (Kvien, Patel and Strand, 2022[80]). A recent analysis of biosimilar uptake in the United States, Germany, and Switzerland found that more biosimilars have been marketed in Germany and Switzerland than in the United States between 2011 and 2020 (Carl et al., 2022[81]). Moreover, the biosimilar market share at launch was highest in Germany, yet it increased at the fastest rate in the United States. Monthly treatment costs of biosimilars in the United States were a median of 1.94 and 2.74 higher than corresponding costs in Germany and Switzerland, respectively.

Policies aimed against anticompetitive practices, addressing patient and physician concerns as well as removing incentives for using more expensive treatment options have been suggested to improve situtation in the United States (Carl et al., 2022[81]; Kvien, Patel and Strand, 2022[80]).

Although substitution policies can generate significant savings, a majority of countries do not mandate substitution for generics and few countries mandate it for biosimilars

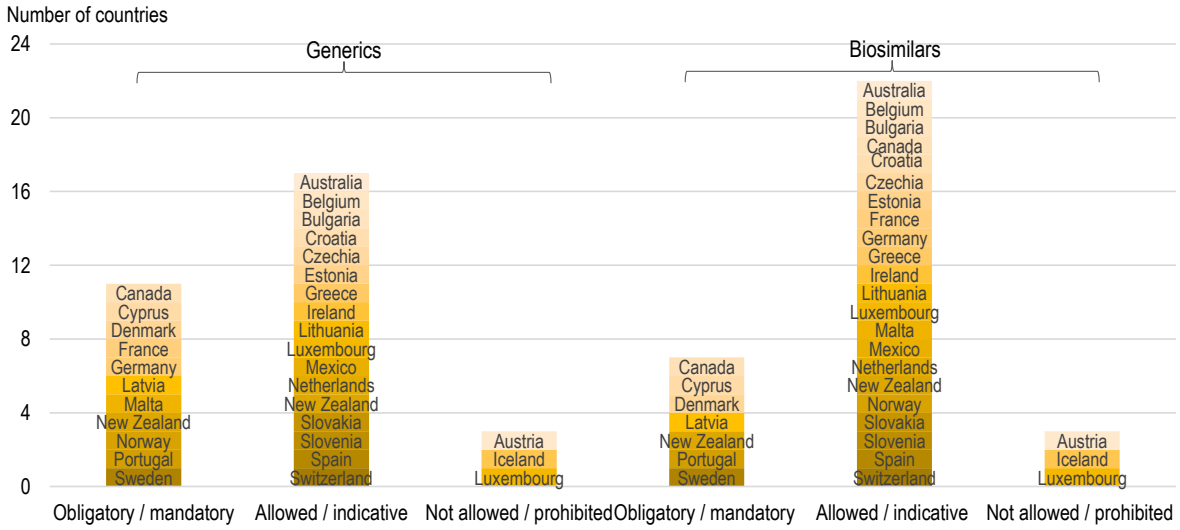
68. Substitution policies may also influence the uptake of generics and biosimilars. Substitution in this context refers to the practice of dispensing/using a medicine instead of another equivalent and interchangeable medicine which has been prescribed without consulting the prescriber (Moorkens et al., 2017[73]). The rationale behind substitution is to ensure that patients receive the cheapest product, which might often be a generic or biosimilar, instead of the originator product. From a medical perspective, substitution for generics is uncontroversial because generics contain the identical chemical substance as the originator product. Substitution for biosimilars has been debated since the first approval of a biosimilar by the EMA in 2006 (Kurki et al., 2017[82]). The main concern was to what extent biosimilars really are interchangeable with the originator product and confer a similar therapeutic benefit. In September 2022, the EMA and the Heads of Medicines Agencies in the EEA eventually ended this debate by concluding that experience from clinical practice has shown that biosimilars are comparable to their reference products and are therefore interchangeable.[29]

69. Respondents to the 2023 OECD Policy Survey on Cancer Care Performance were asked about the current policy on substitution with generics and biosimilars for treatment-naïve patients initiating treatment in oncology; see Figure 4.8. The results show that substitution is allowed / indicative in a majority of countries, more so for biosimilars than for generics. However, even if a country allows substitution, there might be nuances between generics and biosimilars. In Belgium, there is free choice of therapy if prescribed in International Nonproprietary Name (INN), which is a practice promoted for generics but not for biosimilars. For generics, substitution is obligatory / mandatory in 11 countries, while for biosimilars this applies in 7 countries. France and Malta are examples where local legislation requires substitution for generics but not for biosimilars. A few countries do not allow substitution. In Croatia, this only applies to biosimilars, whereas for generics it is allowed only in the case of shortages of the prescribed medicine. In Austria, substitution is not allowed, and physicians are not permitted to use INN prescribing. In Luxembourg, substitution is not allowed outside the hospital setting, but it is allowed at the hospital. In Iceland, the treating physician is obligated to prescribe the cheapest option for treatment-naïve patients and substitution (at the pharmacy level) is therefore not highly important.

[29] See https://www.ema.europa.eu/en/news/biosimilar-medicines-can-be-interchanged, accessed July 2023.

Figure 4.8. Substitution policy for generics and biosimilars for treatment-naïve patients initiating treatment

Based on responses from 28 countries (one option possible for generics and biosimilars, respectively, per country).



Notes: In Canada, the generic substitution policy allows for the substitution of a brand-name drug with an equivalent generic drug, provided certain conditions are met. The conditions may vary depending on the province or territory. For example, a province/territory may require that the pharmacist notifies the patient or prescribing healthcare provider of the substitution. The substitution policy on biosimilars in Canada varies by province and territory, and many provinces and territories require that patients enrolled in the public drug program be prescribed a biosimilar over a reference product for treatment-naïve patients initiating treatment. In Luxembourg, substitution of generics and biosimilars is "allowed / indicative" at the hospital and "not allowed / prohibited" outside the hospital. In New Zealand, the supplier winning the tender is guaranteed up to 95% of the total funded market for a pre-specified amount of time and treatment-naïve patients are required to commence on the winning product, yet this leaves some small allowance for substitution.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

70. Apart from pricing and substitution policies described above, other policies might also be applied to encourage the utilisation of generics and biosimilars. This includes the practice of INN prescribing, where the INN instead of a brand name must be used for prescribing. Financial incentives for physician upon reaching a certain quota of prescribing and dispensing generics/biosimilars could also be implemented (Godman et al., 2019[69]; Moorkens et al., 2017[73]; Vogler et al., 2021[72]).

5 Conclusions and policy options

71. Ensuring equal patient access to a growing number of cancer medicines while balancing the mounting financial pressure is a current major challenge for health systems. The acceleration of the launch of new cancer medicines during the past 20 years is a welcome development. The introduction of new and more effective cancer medicines is needed to reduce the disease burden of cancer and improve the survival prospects of patients. However, constrained health budgets struggle to keep up with this rapid development, not least because of increasing prices of new medicines. The increasing number of cancer patients puts additional demand side pressure on health budgets.

72. In the 2023 OECD Policy Survey on Cancer Care Performance, most countries indicated that the budget impact of new cancer medicines is increasingly influencing their coverage/reimbursement decisions. To manage the budget impact, it is critical to ensure 'value-for-money' through the systematic use of HTA in the pricing and reimbursement process. Healthcare systems need to weigh the costs from investing in cancer medicines against the potential improvements in patient outcomes. An increased focus on spending on effective and cost-effective medicines should be considered. A formal HTA, assessing both effectiveness and costs, should be conducted for all new medicines and extensions to new indications.

73. Another policy option to manage the increasing budget impact is to capitalise on joint/collaborative European HTA to expedite public reimbursement/coverage decisions and to explore cross-border joint procurement. The increasing number of new cancer medicines/indications is intensifying the workload for HTA agencies and pricing and reimbursement bodies. Joint evaluations of (relative) effectiveness of selected cancer medicines by regional cooperations, such as BeNeLuxA and FINOSE, have already been conducted. The joint European HTA applicable from January 2025 for cancer medicines should be used as an opportunity to decrease work at the national level on assessment of (relative) effectiveness rather than result in a duplication of work. Cross-border joint procurement of new cancer medicines could also be explored to achieve lower prices, drawing on previous experiences with COVID-19 vaccines.

74. Many new cancer medicines come to the market with limited/immature evidence on efficacy and cost-effectiveness. This creates a trade-off for public healthcare payers between providing early patient access to new, promising medicines and ensuring solid evidence about the value to patients and society. Therefore, policies to address uncertainty in coverage and/or pricing decisions are growing in importance. According to the 2023 OECD Policy Survey on Cancer Care Performance, nearly all countries reported using financial MEAs to manage uncertainties. The exact implementation differs between countries and medicines within a country but could for instance include (confidential) rebates/discounts, price-volume agreements, or expenditure caps. More than half of the countries also reported the use of performance-based MEAs. Performance-based MEAs may seem more appealing because of their ability to link health outcomes to payments, although their use is currently limited to few situations. Their routine implementation for a wide range of medicines/indications is hampered by the additional administrative burden and/or lack of appropriate IT systems and staff. Functional systems where relevant data can be easily extracted from medical records and processed by healthcare payers would be needed. Financial MEAs might be the only feasible option for most countries and the majority of cancer medicines in the foreseeable future.

75. An important finding of the 2023 OECD Policy Survey on Cancer Care Performance is that the coverage/reimbursement and the time to coverage of cancer medicines varies substantially across

EU/EEA/CH countries. Drawing on a sample of indications with high clinical benefit in breast and lung cancer, Germany reported that all indications were covered, followed by the Netherlands (92%), and Bulgaria and Sweden (both 85%). Apart from Malta with no reimbursed indications, Cyprus and Latvia reported the smallest proportion of indications covered (both 31%). The time from EMA authorisation until national reimbursement/coverage ranged from around 100 days or less in Germany and Sweden to over 1100 days in Cyprus, Latvia, and Lithuania. Moreover, expenditure on cancer medicines (based on list prices) ranged from EUR 13 per capita in Latvia to EUR 108 capita in Austria in 2018. Eastern and Central European countries tend to have a lower utilisation – both measured in value and volumes – of novel cancer medicines.

76. A prioritisation of medicines/indications with a high relative clinical benefit for coverage/reimbursement could help to manage the overall budget impact. Not all new medicines are equally effective. Especially less affluent countries could redirect their limited resources to the most promising treatment alternatives, which would help to mitigate differences in patient outcomes with more affluent countries. Value frameworks, such as the ESMO-MCBS, have been developed to support the process of HTA and to assist in rationalising reimbursement decisions. New medicines with a potentially high clinical benefit could be reviewed on a fast-track basis and prioritised for coverage/reimbursement, whereas new medicines with a potentially low clinical benefit could de-prioritised. Alternatively, reimbursement/coverage could be applied to a smaller patient population than the one defined in the marketing authorisation. Such restrictions in coverage are already applied in some countries to focus on subgroups of patients that derive the highest clinical benefit.

77. The treatment of cancer with medicines is becoming increasingly individualised, moving away from a one-size-fits all approach based on the tissue where the tumour originated. Between 2015 and 2020, almost half of new indications targeting solid tumours were approved based on a biomarker. Biomarker testing is therefore critical to identify the right patients for a targeted treatment. According to the 2023 OECD Policy Survey on Cancer Care Performance, a majority of countries indicated that the coverage/reimbursement of companion diagnostics is not automatically coupled to the coverage of medicines. This can lead to a paradoxical situation in which a medicine is reimbursed but its companion diagnostic is not. Such an environment may slow the adoption of 'personalised medicine' in clinical practice and potentially put a financial burden on patients who pay out-of-pocket for the biomarker testing. Countries should ensure that the reimbursement of a companion diagnostic always occurs in an integrated way with the reimbursement of the medicine. Additional costs of both the biomarker testing and the use of the new medicine need to be incorporated in the HTA process. Apart from the joint reimbursement of the companion diagnostic and the medicine, countries should also ensure adequate public budgets so that all eligible patients can access the testing and the medicine. To facilitate the adoption in clinical practice, it is also important to update local clinical guidelines and protocols, provide continuous training of clinical staff, and ensure adequate infrastructure and staff for diagnostic testing and treatment administration.

78. Clinical trials and early access schemes offer patients an opportunity to receive new cancer medicines before regulatory approval and/or reimbursement approval. However, the availability of clinical trials in oncology ranges from fewer than 2 trials to more than 10 trials per 100,000 inhabitants across the EU, with poorer access in Eastern and Central Europe. According to the 2023 OECD Policy Survey on Cancer Care Performance, many countries use early access systems to improve access to novel cancer medicines despite limited/immature evidence on efficacy. Countries with early access schemes most often provide access on a named-patient basis. This creates inequalities within countries, because named-patient schemes often only benefit a small share (such as fewer than 10%) of clinically eligible patients. In addition, early access schemes using a named-patient approach create administrative burden to handle cases on a one-on-one basis and may only benefit well-informed patients or patients treated by certain physicians. A switch to a population-based system could be explored as it could contribute to reducing inequalities in access.

79. The steep increase in the number of new cancer medicines in the past two decades means that a growing number of medicines will eventually experience patent expiration and/or loss of market exclusivity. The opportunities to achieve savings with generics and biosimilars will rise in the coming years and decades, because generics and biosimilars can lead to substantial price reductions. Experience with three previous blockbuster cancer medicines (bevacizumab, rituximab, trastuzumab) showed that all countries started to reimburse at least one biosimilar for each of the three medicines. Yet the mean time from EMA approval to public reimbursement/coverage exhibited great variations between countries, ranging from around 200 days in Germany and Spain to between 700 and 835 days in Greece, Iceland, Latvia, Lithuania, and Slovenia and almost 1400 days in Cyprus.

80. Different policies exist to stimulate the utilisation and efficient use of generics and biosimilars when they become available in clinical practice. This includes pricing policies of various forms. Reference price systems for both generics and biosimilars are in place in a majority of countries according to results from the 2023 OECD Policy Survey on Cancer Care Performance. These policies can help to control prices of both the generics/biosimilars and the reference medicine after loss of market exclusivity. Moreover, the adoption of generics and in particular of biosimilars in clinical practice might be somewhat hampered by policies that do not allow or encourage substitution for the reference medicine. Although substitution policies can generate significant savings, a majority of countries does not mandate substitution for generics and few countries mandate it for biosimilars. For biosimilars, the previous debate about interchangeability with the reference medicine was ended in favour of biosimilars by the EMA and the Heads of Medicines Agencies in the EEA in September 2022. Therefore, mandatory substitution for the cheapest generic/biosimilar for cancer patients initiating treatment should be considered. This would help to stimulate competition between producers of generics and biosimilars and may create considerable budget headroom, which can be reinvested in new cancer medicines that offer substantial clinical benefits to patients.

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Annex A. Analysis of newer cancer medicines with high clinical benefit

Table A A.1. Selection algorithm for indications of newer cancer medicines with high clinical benefit

Criteria	Number of indications	Comment
1. Indications with ESMO-MCBS A or 5 on 26th March 2023	61	
2. Indications with EMA marketing authorisation after 1st January 2016	28	This excludes indications prior to the introduction of ESMO-MCBS in 2015; ESMO-MCBS has only been more systematically employed to EMA-approved indications since 1st January 2016
3. Indications with valid EMA marketing authorisation on 26th March 2023	27	This excludes indications that were withdrawn or have been replaced
4. Indications used in the curative setting or as first-line treatments in the non-curative setting	22	This excludes indications approved as second-line treatments for advanced disease in the non-curative setting
5. Indications in breast cancer and lung cancer	10	Excludes indications in all cancer types except breast and lung cancer

Notes: The final 10 indications in lung cancer and breast cancer were grouped by indication (see Table A A.3). Similar indications of other newer medicines of the same drug class were added even if they had a lower ESMO-MCBS score. This concerned cemiplimab in the treatment of metastatic non-small cell lung cancer with a high expression of PD-L1 as well as abemaciclib and palbociclib in the treatment of metastatic hormone-sensitive HER2-negative breast cancer. The total number of indications analysed thus was 13.
Sources: ESMO-MCBS was obtained from https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-scorecards (accessed 26th March 2023) and EMA authorisations were obtained from https://ec.europa.eu/health/documents/community-register/html/index_en.htm (accessed 26th March 2023).

Table A A.2. Indications of newer cancer medicines with high clinical benefit used in the analysis

International non-proprietary name (INN)	Brand name	EMA marketing authorisation date	EMA-approved indication (label)	Cancer type	ESMO-MCBS
abemaciclib	Verzenios	2018-09-27	in combination with an aromatase inhibitor or fulvestrant for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in as initial endocrine-based therapy, or in women who have received prior endocrine therapy. In pre- or perimenopausal women, the endocrine therapy should be combined with a LHRH agonist.	breast	3/4
abemaciclib	Verzenios	2022-04-01	in combination with endocrine therapy for the adjuvant treatment of adult patients with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative, node positive early breast cancer at high risk of recurrence. In pre or perimenopausal women, aromatase inhibitor endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist.	breast	A
atezolizumab	Tecentriq	2021-04-30	as monotherapy for the first-line treatment of adult patients with metastatic non-small cell lung carcinoma (NSCLC) whose tumours have a PD-L1 expression ≥ 50% TC or ≥ 10% tumour-infiltrating immune cells (IC) and who do not have EGFR mutant or ALK-positive NSCLC	lung	5
atezolizumab	Tecentriq	2022-06-07	as monotherapy as adjuvant treatment following complete resection and platinum-based chemotherapy for adult patients with non-small cell lung carcinoma (NSCLC) with a high risk of recurrence whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and who do not have EGFR mutant or ALK positive NSCLC	lung	A
cemiplimab	Libtayo	2021-06-21	as monotherapy for the first-line treatment of adult patients with non-small cell lung cancer (NSCLC) expressing PD-L1 (in ≥ 50% tumour cells), with no EGFR, ALK or ROS1 aberrations, who have locally advanced NSCLC who are not candidates for definitive chemoradiation, or metastatic NSCLC	lung	4
olaparib	Lynparza	2022-08-02	as monotherapy or in combination with endocrine therapy for the adjuvant treatment of adult patients with germline BRCA1/2-mutations who have HER2-negative, high risk early breast cancer previously treated with neoadjuvant or adjuvant chemotherapy	breast	A
osimertinib	Tagrisso	2021-05-21	as monotherapy as adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA non-small cell lung carcinoma (NSCLC) whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations	lung	A

palbociclib	Ibrance	2016-11-09	for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer: - in combination with an aromatase inhibitor; - in combination with fulvestrant in women who have received prior endocrine therapy (see section 5.1). In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.	breast	3/4
pembrolizumab	Keytruda	2017-01-27	as monotherapy for the first-line treatment of metastatic non-small cell lung carcinoma (NSCLC) in adults whose tumours express PD-L1 with a ≥50% tumour proportion score (TPS) with no EGFR or ALK positive tumour mutations	lung	5
pembrolizumab	Keytruda	2022-05-19	in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, for the treatment of adults with locally advanced, or early stage triple negative breast cancer at high risk of recurrence	breast	A
pertuzumab	Perjeta	2018-05-31	in combination with trastuzumab and chemotherapy in the adjuvant treatment of adult patients with HER2-positive early breast cancer at high risk of recurrence	breast	A
ribociclib	Kisqali	2018-12-17	in combination with endocrine-based therapy for the treatment of premenopausal women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer. In pre or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone releasing hormone (LHRH) agonist.	breast	5
trastuzumab emtansine	Kadcyla	2019-12-16	as monotherapy for the adjuvant treatment of adult patients with HER2-positive early breast cancer who have residual invasive disease, in the breast and/or lymph nodes, after neoadjuvant taxane-based and HER2-targeted therapy	breast	A

Note: The 13 indications contain the 10 indications selected according to Table A A.1 and 3 indications of other, similar medicines with lower ESMO-MCBS but that concern the same patient group.

Table A A.3. Indications of newer cancer medicines with high clinical benefit with public reimbursement/coverage as of 1st April 2023

Indication	INN	AT	BE	BG	HR	CY	CZ	DK	EE	FR	DE	EL	HU	IS	IE	LV	LT	MT	NL	NO	PL	PT	SI	ES	SE	CH
Breast, HR+ HER2-, metastatic	abemaciclib	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	palbociclib	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	ribociclib	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Breast, HR+ HER2-, early-stage adjuvant	abemaciclib	No	No	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	No	No	No	No	No	Yes	No	No	No	Yes	No	Yes	No
Breast, HER2+, early-stage adjuvant	pertuzumab	Yes	Yes	Yes	Yes	No	Yes	No	No	No	Yes	Yes	No	Yes	No	No	No	No	Yes	Yes	No	No	Yes	No	No	Yes
	trastuzumab emtansine	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Breast, TNBC, early-stage neo/adjuvant	pembrolizumab	Yes	Yes	Yes	No	No	Yes	Yes	No	No	Yes	No	No	Yes	No	No	No	No	Yes	No	No	No	Yes	No	Yes	No
Breast, BRCA+, early-stage adjuvant	olaparib	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes
Lung-NSC, PD-L1-high, metastatic	atezolizumab	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	cemiplimab	Yes	Yes	No	No	No	No	Yes	No	Yes	Yes	No	No	No	No	No	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
	pembrolizumab	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Lung-NSC, PD-L1-high, early-stage adjuvant	atezolizumab	Yes	Yes	Yes	No	No	Yes	Yes	No	No	Yes	No	No	Yes	No	No	No	No	Yes	No	No	No	No	No	Yes	Yes
Lung-NSC, EGFR+, early-stage adjuvant	osimertinib	No	No	Yes	No	No	Yes	No	Yes	No	Yes	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes	No	No	Yes	Yes	No

Notes: Yes = reimbursed, No = not reimbursed on 1st April 2023. Medicines are grouped by similar indications.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

Annex B. Analysis of biosimilars of cancer medicines

Table B B.1. Biosimilars used in the analysis

International non-proprietary name (INN)	Brand name	EMA marketing authorisation date
bevacizumab	Mvasi	2018-01-15
bevacizumab	Zirabev	2019-02-14
bevacizumab	Aybintio	2020-08-19
bevacizumab	Onbevzi	2021-01-11
bevacizumab	Oyavas	2021-03-26
bevacizumab	Alymsys	2021-03-26
bevacizumab	Abevmy	2021-04-21
bevacizumab	Vegzelma	2022-08-17
rituximab	Truxima	2017-02-17
rituximab	Riximyo	2017-06-15
rituximab	Rixathon	2017-06-15
rituximab	Blitzima	2017-07-13
rituximab	Ruxience	2020-04-01
trastuzumab	Ontruzant	2017-11-15
trastuzumab	Herzuma	2018-02-09
trastuzumab	Kanjinti	2018-05-16
trastuzumab	Trazimera	2018-07-26
trastuzumab	Ogivri	2018-12-12
trastuzumab	Zercepac	2020-07-27

Sources: EMA authorisations were obtained from https://www.ema.europa.eu/en/medicines/download-medicine-data (accessed 26th March 2023).

Table B B.2. Biosimilars for cancer medicines with public reimbursement/coverage as of 1st April 2023

INN	Brand name	AT	BE	BG	HR	CY	CZ	DK	EE	FR	DE	EL	HU	IS	IE	LV	LT	MT	NL	NO	PL	PT	SI	ES	SE	CH
bevacizumab	Mvasi	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
bevacizumab	Zirabev	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes
bevacizumab	Aybintio	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	No	No	Yes	Yes	No
bevacizumab	Onbevzi	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No
bevacizumab	Oyavas	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
bevacizumab	Alymsys	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
bevacizumab	Abevmy	Yes	Yes	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	No	No	Yes	No	Yes	No	Yes	No
bevacizumab	Vegzelma	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	No	No	No	No	No	No	No	Yes	No	No	Yes	No	Yes	Yes	No
rituximab	Truxima	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes
rituximab	Riximyo	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	No	No
rituximab	Rixathon	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
rituximab	Blitzima	No	No	No	No	No	No	No	Yes	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No	No	No
rituximab	Ruxience	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No

trastuzumab	Ontruzant	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No
trastuzumab	Herzuma	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	No	Yes
trastuzumab	Kanjinti	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
trastuzumab	Trazimera	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
trastuzumab	Ogivri	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
trastuzumab	Zercepac	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No

Notes: Yes = reimbursed, No = not reimbursed on 1st April 2023.
Source: Authors based on the 2023 OECD Policy Survey on Cancer Care Performance.

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