EXECUTIVE SUMMARY

KRAKOW, WARSAW, BUDAPEST 2022

GEARING UP

IMPROVING TIME TO PATIENT ACCESS TO INNOVATIVE THERAPIES IN V4

POLAND • CZECHIA • SLOVAKIA • HUNGARY

G.A.P.

GEARING UP ACCESS PROPOSAL FOR V4

AUTHORS:
MAGDALENA WŁADYSIUK
ROBERT PLISKO
KAJA KOSTRZEWSKA
ÁGNES TÓTH
MARK MOLNAR

DATA ANALYSIS:
ROBERT PLISKO
KAJA KOSTRZEWSKA

DESIGN AND ILLUSTRATIONS:
KATARZYNA KAPCIA

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AZ ÚJ GYÓGYSZER ÚJ ESÉLY

efpia

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i&s Ideas & Solutions

hta consulting

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ABOUT THE PROJECT

This international project aims to analyze and compare the gaps and successes in patient access to new treatments among the Visegrád Group countries based on the European average or clinical standards. A further ambition is to establish stakeholder cooperation across Europe on monitoring patient access to new treatments approved by EMA by creating a platform for discussion. Our holistic approach intends to analyze patient access using a multidimensional methodology to provide quantified explanation for reasons behind lack of patient access when this occurs. Whilst there have been many attempts across Europe to measure patient access, **our project's uniqueness is tangible as we adapted the frequently used indicators regarding the specific characteristics of the Central and Eastern European (CEE) region and developed additional dimensions especially fitting to our geography.**

Although significant improvements have been observed in the last two decades with respect to access to innovative therapies among CEE countries, there are several further critical points still to be taken care of in order to provide the most optimal treatments in the region. **The GAP (GEARING UP ACCESS PROPOSAL FOR V4) tool prudently measures the level of access to novel medicines among selected therapeutic areas in Visegrád Group (V4) countries (Poland, Hungary, Czechia, and Slovakia).** The performed analysis allows identification of certain still existing concerns in the availability to care, measurement of the positive impact of recent national drug policy interventions, and our results provide a good basis for further evidence-based policy making in the respective countries to develop the national drug reimbursement systems further.

This report presents the outcomes of the "GAP Gearing up to Patient Access" initiative for Visegrád Group in a form of a set of quantified indicator values. After meticulous analysis of available source data from Visegrád Group countries applying a multidimensional methodology, we associated aggregated value scores to each focus dimensions, therapy areas and countries. Our results allow us not only to compare the performance of Visegrád Group countries on aggregated level, but we can also compare specific therapy areas between countries, or one specific therapy area with another one within a respective country. The multidimensional notion of our methodology tailored to Central and Eastern Europe allows us to pick certain dimensions and to make flexible comparisons to identify national successes or lags.

The GAP project was initiated by EMployers' Union of Innovative Pharmaceutical Companies Poland (INFARMA) and Association of Innovative Pharmaceutical Manufacturers Hungary (AIPM) and financed from European Federation of Pharmaceutical Industries and Associations (EFPIA) grant. INFARMA is an association of 25 companies from the pharmaceutical industry in Poland, launched in 1993, AIPM is an association of 26 pharmaceuticals companies in Hungary established in 1992. The project was carried out with the support of Ideas&Solutions team from Hungary and HTA Consulting from Poland. Our analysis was supported by Pharmeca team related to Czech and Slovak data collection. This publication is the summary of the main results of the project based on data collected for 2020-2021 for Visegrád Group countries.

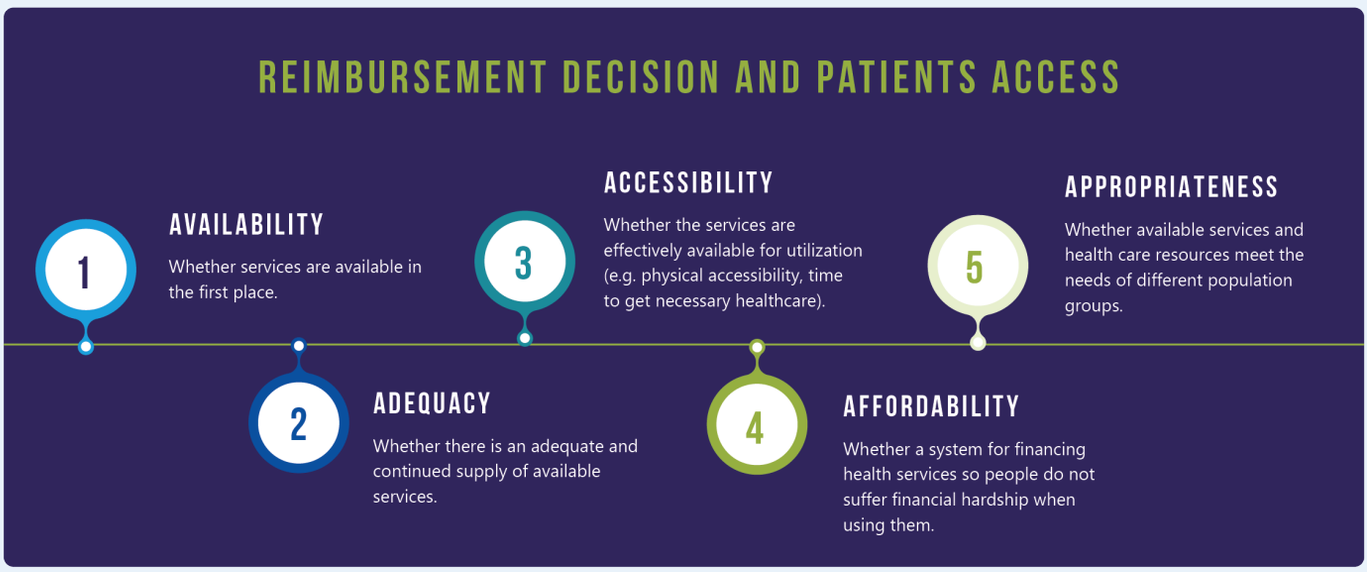
GLOSSARY

DALY	Disability adjusted life-years.
KPI *Key Performance Indicators*	We have developed a multi-level indicator framework in which indicators are aggregated for each general indication and for each country. As a result, making it possible to compare several aspects of access to therapies and diagnostic procedures in a multidimensional way. All therapy areas have been evaluated using the same set of 8 indicators, taking into account different aspects of patient access including availability, affordability and accessibility of pharmaceutical products, as well as diagnostics. However, all indicators have been adapted to the specific therapy areas in terms of relevant products and diagnostic tests.
V4 - VISEGRÁD GROUP	The Visegrád Group, Visegrád Four, V4, or the European Quartet, is a cultural and political alliance of four countries in Central Europe - Czech Republic, Hungary, Poland and Slovakia, which are members of the EU and of NATO, to advance co-operation in military, cultural, economic and energy matters with one another and to further their integration with the EU.

EXECUTIVE SUMMARY

INTRODUCTION

Improving the availability of medicines authorised in the European Union (EU) is a key priority for the European medicines regulatory network and for the pharmaceutical industry according to the new Pharmaceutical Policy in the EU. Member State countries, in line with the health national policies, are gearing up for universal coverage in the healthcare sector, including equalisation of the access to medicines. These objectives need to take account the "lifecycle" of a pharmaceutical product and the different regulatory levers and policy interventions that take place over its course. In recent years, policymakers in European countries have been increasingly concerned about developments in the pharmaceutical sector that have been challenging the affordability of new medicines and the financial sustainability of solidarity in the publicly funded health care systems[1,2]. The '5 As' definition is widely used to capture the different aspects of patient access, including availability, adequacy, accessibility, affordability and appropriateness[4,5,6].



[1] *World Health Organization. Regional Office for Europe, Policies EO on HS and, Vogler S, Paris V, Panteli D. Ensuring access to medicines: how to redesign pricing, reimbursement and procurement?. 2018*

[2] *Godman B, Hill A, Simoens S, Selke G, Selke Krulichová I, Zampirolli Dias C, Martin AP, Oortwijn W, Timoney A, Gustafsson LL, Voncina L, Kwon H-Y, Gulbinovic J, Gotham D, Wale J, i in. (2021) Potential approaches for the pricing of cancer medicines across Europe to enhance the sustainability of healthcare systems and the implications. Expert Rev. Pharmacoecon. Outcomes Res. 21(4):527–540.*

[3] *Penchansky R, Thomas JW. The concept of access: definition and relationship to consumer satisfaction. Med Care. 1981;19(2):127-140.*

[4] *The model by Penchasky & Thomas was readapted by the multi-stakeholder Patient Access Partnership (PACT) network and the same approach was accepted by the European Patients Forum in 2016. 5As are complemented by „Timeliness" in the Towards a fairer and more effective measurement of access to healthcare across the EU report.*

[5] *Garcia MM, Barbosa MM, Silva RM, Reis EA, Alvares J, Assis Acurcio F de, Godman B, Guerra Junior AA. (2019) Indicator of access to medicines in relation to the multiple dimensions of access. J. Comp. Eff. Res. 8(12):1027–1041.*

[6] *Barbosa MM, Moreira TA, Nascimento RC, Nascimento MM, Acurcio FA, Godman B, Guerra AA, Alvares-Teodoro J. (2021) Access to medicines in the Brazilian Unified Health System's primary health care: assessment of a public policy. J. Comp. Eff. Res. 10(10):869–879.*

Access to new therapies and diagnostics varies significantly between countries in the EU. This has been seen with the utilisation of new biological medicines to treat immune diseases, including rheumatoid arthritis and inflammatory bowel diseases[7,8,9]. In addition, for medicines to treat rare diseases and cancer[10]. The importance of attaining affordable access to pharmaceutical products in the global efforts towards universal health coverage has long been recognized. The increasing wave of scientific innovation approved by EMA over the last 10 years could generate substantial health benefit on a population level. Between 2010 and 2021, six hundred sixty new molecules (excluding generics and biosimilars) have been launched onto the EU market with EMA approval. One hundred twenty-three of these new medicines are for oncology indications. They represent 27% of all registered molecules. 19% of new medicines have an orphan designation. 12% are used in metabolic diseases, including 35 molecules indicated for diabetes mellitus.

A new Pharmaceutical Strategy, adopted in October 2021 by the EU Commission, promises patient access to affordable medicines and aims to support competitiveness and innovation in Europe's pharmaceutical industry. To ensure access to affordable medicines for patients, it also addresses unmet medical needs (e.g. oncology, rare diseases) and promotes a high level of quality, efficacy and safety standards.

In Europe, multiple organizations have developed and/or published healthcare indicators, ranging from large-scale, regularly updated databases and reports[11] to ad hoc, disease-specific surveys and reviews commissioned by authorities, patient associations or commercial projects. **In this project, a unique multi-level indicator framework for measurement of patient access to therapies and diagnostics was developed by a group of experts. Its aim is to create a benchmark for the V4 region from the angle of clinical standards with the same set of 8 indicators capturing different aspects of patient access, including availability, affordability, and accessibility of pharmaceutical products, as well as diagnostics. All indicators were adapted to specific therapeutic areas in terms of relevant medicines and diagnostic tests.** At the highest level of analysis, to give an overall assessment, a single cumulative indicator was calculated for each country, based on the disease-level indicators. **It allows us to draw direct comparisons between the**

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[7] *Putrik P, Ramiro S, Kvien TK, Sokka T, Pavlova M, Uhlig T, Boonen A, Working Group 'Equity in access to treatment of rheumatoid arthritis in Europe'. (2014) Inequities in access to biologic and synthetic DMARDs across 46 European countries. Ann. Rheum. Dis. 73(1):198–206.*

[8] *Baumgart DC, Misery L, Naeyaert S, Taylor PC. (2019) Biological Therapies in Immune-Mediated Inflammatory Diseases: Can Biosimilars Reduce Access Inequities? Front. Pharmacol. 10:.*

[9] *Kostić M, Djakovic L, Šujić R, Godman B, Janković SM. (2017) Inflammatory Bowel Diseases (Crohn´s Disease and Ulcerative Colitis): Cost of Treatment in Serbia and the Implications. Appl. Health Econ. Health Policy. 15(1):85–93.*

[10] *EURORDIS. (2018) Breaking the Access Deadlock to Leave No One Behind. Dostęp: http://download2.eurordis.org.s3.amazonaws.com/positionpapers/eurordis_access_position_paper_final_4122017.pdf.*

[11] *e.g., Euro Health Consumer Index by Health Consumer Powerhouse; European Core Health Indicators and Eurostat data by EU; OECD Health data and reports; WHO Health reports and Core Health Indicators in the WHO Europe Region; measurements by national authorities etc.*

healthcare systems in V4 in the investigated areas.

Better access to the diagnostic procedures and therapies is one the key elements within the entire healthcare service system, which is necessary to improve survival and quality of life (as measured in DALY) in a given population. All disease areas selected for the purposes of the current project are important from the public health perspective (Table 1).

The medicines selected for the analysis represent close to 20% of all EMA-registered medicines over the horizon considered, which we believe represent an adequate sample to illustrate the extent of any lack of reimbursement or availability in the V4 countries. Despite the similarities of these countries, at least several differences can be observed in medicine accessibility. Currently, three dimensions of patient access can be found among the Visegrád Group:

1. Out of all included therapies with a European marketing authorization in selected diseases, the proportions of therapies that received Market Access, i.e. are reimbursed through social health insurance schemes, range from as low as 11% to as high as 69%.
2. Following European marketing authorization, the time to Market Access ranges from as low as 53 days to almost 3,300 days.
3. Share of patients on a specific novel treatment in 2020 ranges from as low as 0% to as high as 58%.

#	KPI		5 "A"
1	RESTRICTIONS ON REIMBURSEMENT	THERAPY	Accessibility **Availability**
2	TIME TO AVAILABILITY		Accessibility
3	COMPLIANCE WITH INTERNATIONAL GUIDELINES		**Availability** Adequacy Accessibility
4	EARLY ACCESS PROGRAMS		Accessibility
5	SHARE OF PATIENTS ON A SPECIFIC NOVEL TREATMENT		Accessibility Appropriateness
6	NOVEL TREATMENT DEPLOYMENT		**Availability** Adequacy Appropriateness
7	REIMBURSEMENT OF MOLECULAR TESTS	DIAGNOSTICS	Adequacy Accessibility
8	ACCESS TO ADVANCED DIAGNOSTICS		Adequacy Accessibility

In view of such discrepancies, the aim of the present analysis is to facilitate a better understanding of these deeply complex issues. Our results may be hopefully supporting for decision makers and other stakeholders in preparing for future innovations in healthcare among the V4 countries and how these may become more accessible. The disclosed differences may become motivators to promote equal access to health care across the V4 countries as well as to show key stakeholders potential actions for improvement where there are concerns.

IT IS TIME TO ACT.

VISEGRÁD GROUP COUNTRIES

The V4 countries in Central-Eastern Europe have been cooperating for almost 30 years. Today, bilateral or multilateral cooperation exists at the highest level between V4 leaders, and is considered well organised at the international arena The Visegrád Group reflects the efforts of the countries of the Central European region to work together in a number of fields of common interest within an all-European integration.

The V4 is not just a group of 4 countries, it is a population of over 64,9 million people, who have access to universal public health care. All members of the Visegrád Group have a system of statutory health insurance based on compulsory membership in a health insurance fund or funds. Yet, only in Czechia the public health coverage was 100% in 2018. In Slovakia and Hungary the insurance coverage was 94.6% and 94.0% respectively. Poland has 92.9% of its population is covered for health services[12]. Healthcare spending in V4 countries has grown over time. However despite this, current

[12] *OECD. (2020) Population coverage for a core set of services, 2018 (or nearest year). Paris: Organisation for Economic Co-operation and Development Dostęp: https://www.oecd-ilibrary.org/social-issues-migration-health/population-coverage-for-a-core-set-of-services-2018-or-nearest-year_db6084a4-en (8.12.2021).*

spending as a proportion of GDP is still less than the mean of the EU27 countries by approximately 3 percentage points. This difference in public healthcare spending has been consistent over several past years creating more challenges in drug policies.

As in most European countries, price negotiations, assessment and appraisal take place on a national level among the Visegrád Group of countries; however, budgets are allocated by healthcare insurers (a single payer institution or different health insurers) or on a hospital level. The Visegrád Group of countries already cooperate on areas of healthcare. This includes exchanging experiences and good practices regarding the reimbursement processes carried out in particular countries as well as in the field of the pricing policy.

VISEGRÁD GROUP

GOALS & METHODOLOGY OF THE PROJECT

Ensuring patient access is the key determinant to deliver value of innovative treatments to further improve the health of the population health. Universal coverage and access to pharmaceutical innovations have appreciably improved patient outcomes across the different indications. However, this can only be achieved by full access to advances on health care.

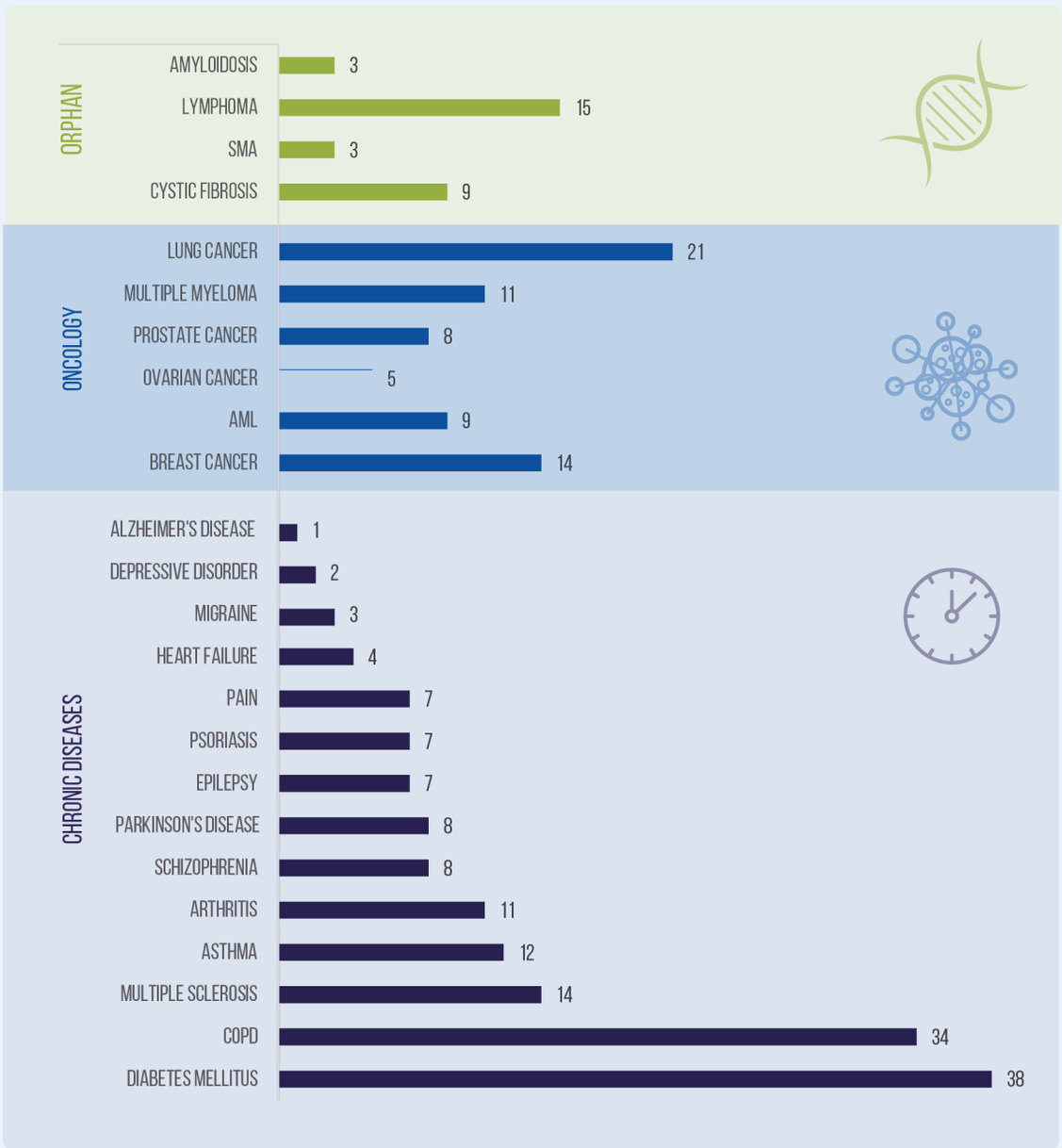
Our goal is to support key decision makers to identify the gaps in patient access to innovative therapies throughout the Visegrád Group countries.

To present different dimensions of patient access, we selected a total of 10 indications (therapy areas) divided in 3 categories: oncology, chronic diseases and rare diseases. These categories may serve as representative examples for describing and evaluating patients' access to innovative therapies in the Visegrád Group countries. Evaluated therapy areas were those for which the highest number of new innovative treatments had been approved in Europe between 2010 and 2021; consequently, it was possible to assess the extent to which they have become available to patients in actual practice.

As the first step, diseases were divided into three areas described above. In each of these areas, individual diseases were selected for further analysis on the basis of the highest number of medicines registered by the EMA. Therapy areas selected for gap assessment are as follows: breast cancer, non-small-cell lung cancer (NSCLC), ovarian cancer and prostate cancer in oncology; acute myeloid leukemia (AML), lymphoma (multiple types), spinal muscular atrophy (SMA), and cystic fibrosis in rare diseases; and diabetes mellitus and multiple sclerosis (MS) in the 'other' chronic disease category.

All therapeutic areas are evaluated using the same set of 8 indicators which capture different aspects of patient access, including availability, affordability, and accessibility of innovative pharmaceutical products, treatments recommended by clinical guidelines as well as diagnostics; furthermore, real-life utilization of selected therapies was also considered. All indicators were adapted to the specific therapeutic area in terms of relevant pharmaceutical products and diagnostic tests.

NUMBER OF REGISTERED NOVEL ACTIVE SUBSTANCES BY EMA BETWEEN 2010-2021



AML – Acute Myeloid Leukemia, COPD – Chronic Obstructive Pulmonary Disease, SMA – Spinal Muscular Atrophy

Patient access indicators are descriptive measurements that evaluate the level of patient access by defining a set of benchmarks comparing several aspects of treatment and diagnostic process. After conducting a review of existing and publicly available patient access indicators in international measurements, we developed a multi-level indicator framework in which indicators are aggregated for each therapeutic area and for each country. As a result, making it possible to compare diseases and countries in a flexible way.

Data on which indicators are based on those published by national authorities in each country, including national reimbursement databases, reimbursement protocols, and prescription databases. Furthermore, we used international guidelines published by professional organizations as a benchmark. In cases when certain necessary data points were not publicly available for all countries, we used estimates based on the available data.

#	INDICATOR (KPI) NAME	DESCRIPTION AND RATIONALE
1	RESTRICTIONS ON REIMBURSEMENT	refers to the availability of reimbursed treatment options at the country level by calculating the proportion of innovative medicines approved by EMA that are available under the regular or irregular reimbursement. Partial reimbursement (restrictions compared to EMA label) is given less weight than a full indication reimbursement.
2	TIME TO AVAILABILITY	refers to the length of time (measured as number of days) between the EMA marketing approval and the date of availability under regular reimbursement for patients.
3	COMPLIANCE WITH INTERNATIONAL GUIDELINES	refers to the proportion of therapies reimbursed in a given country. The main points of relevant international guidelines of professional organizations (e.g., ESMO guidelines) were identified for each indication.
4	EARLY ACCESS PROGRAMS	refers to the availability of early access programs (excluding compassionate use) before regular reimbursement. Early access programs are a pathway to provide innovative treatments through individual application in some countries .
5	SHARE OF PATIENTS ON A SPECIFIC NOVEL TREATMENT	refers to the utilization of specific therapies. The indicator refers to the share of patients on a specific innovative treatment (or a category of innovative drugs) in 12 months, compared to the total number of eligible patients. The number of eligible patients is calculated using the same population data e.g. epidemiological data were identified in each indication.
6	NOVEL TREATMENT DEPLOYMENT	refers to the utilization of a specific ATC code category (in absolute value) per total population per 12 months.
7	REIMBURSEMENT OF MOLECULAR TESTS	refers to the public reimbursement of molecular or other tests required when the qualification to the therapy is conditioned by the presence of a specific biomarker. Relevant tests were selected for each indication based on guidelines.
8	ACCESS TO ADVANCED DIAGNOSTICS	refers to the typical waiting time for elective diagnostics following the referral, which may affect the time to treatment initiation or further diagnostics. Relevant diagnostic tests were specified for each indication based on guidelines.

DISEASE BURDEN IN VISEGRÁD GROUP COUNTRIES

All selected diseases are important from a public health perspective and their population burden can be assessed by evaluating the quality of life with increasing disability or loss of life years of the burdened population.

DALY (*Disability Adjusted Life-Years*) is a well-recognised tool, **that allows international comparison between countries to determine the health status of the population[13,14,15]. One DALY represents the loss of the equivalent of one year of full health.** DALYs is the sum of the years of life lost due to premature mortality (YLLs) and the years of years of healthy life lost due to disability (YLDs) for people living in states of less than good health resulting from the specific disease.

INDICATIONS SELECTED FOR ACCESS GAP ASSESSMENT

THE DISEASE WAS SELECTED BASED ON THE 10 YEARS ANALYSIS OF EMA AUTHORIZATION.

ONCOLOGY


NSCLC


BREAST CANCER


PROSTATE CANCER


OVARIAN CANCER

ORPHAN


CYSTIC FIBROSIS


ACUTE MYELOID LEUKEMIA (AML)


LYMPHOMA


SPINAL MUSCULAR ATROPHY (SMA)

CHRONIC DISEASES


DIABETES MELLITUS


MULTIPLE SCLEROSIS (MS)

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[13] *Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Akinyemiju TF, Al Lami FH, Alam T, Alizadeh-Navaei R, Allen C, Alsharif U, Alvis-Guzman N, Amini E, Anderson BO, Aremu O, Artaman A, Asgedom SW, Assadi R, i in. (2018) Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2016: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol. 4(11):1553–1568.*

[14] *Masaebi F, Salehi M, Kazemi M, Vahabi N, Azizmohammad Looha M, Zayeri F. (2021) Trend analysis of disability adjusted life years due to cardiovascular diseases: results from the global burden of disease study 2019. BMC Public Health 21(1):1268.*

[15] *Feigin VL, Nichols E, Alam T, Bannick MS, Beghi E, Blake N, Culpepper WJ, Dorsey ER, Elbaz A, Ellenbogen RG, Fisher JL, Fitzmaurice C, Giussani G, Glennie L, James SL, i in. (2019) Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 18(5):459–480.*

In 2019, selected disease entities accounted for 13% of the total DALY burden among the Visegrád Group countries. Of the 10 diseases selected for analysis two (lung cancer - NSCLC, diabetes) collectively account for more than 70% of the DALY burden generated by the 10 selected diseases. Over 60% of the total DALY burden is generated by oncology (4 indications), while chronic diseases (2 indications) are responsible for 33% of the burden. The remaining 6% of the DALY burden is generated by selected rare diseases (4 indications). Rare diseases separately do not have a significant impact on DALYs. However, they should not be forgotten as there are more than 8 000 of them and that together they cover several percent of the population in a given country. Indeed rare diseases have a very high interest in societies, and sometimes a rare disease affecting a very few patients has greater visibility in among the public, than a conventional chronic illness with millions of patients[16,17].

TOTAL LOSS OF QUALITY LIFE YEARS IN V4 COUNTRIES

[16] *Kole A, Hedley V. (2021) Recommendations from the Rare 2030 Foresight Study: The future of rare diseases starts today, http://download2.eurordis.org/rare2030/Rare2030_recommendations.pdf.*

[17] *EURORDIS. (2018) Breaking the Access Deadlock to Leave No One Behind. Dostęp: http://download2.eurordis.org.s3.amazonaws.com/positionpapers/eurordis_access_position_paper_final_4122017.pdf.*

MAIN RESULTS

In recent years policymakers among European countries have been increasingly concerned about developments in the pharmaceutical sector, the affordability of new medicines and the financial sustainability and solidarity among publicly funded health care systems. The Visegrád Group countries already cooperate in the medical field, which may result in the increased availability of affordable treatment options. The EU Member States use a diversified approach in terms of reimbursement and pricing to determine access to new medicines. Different policies are applied for different sectors, market segments, and medicines. Some pricing, procurement, and reimbursement policies are used more frequently for new, potentially high-priced medicines, including managed entry agreements[18].

For each country, there are therapeutical areas with better or worse access. Overall, the access to medical innovations in Visegrád Group countries is, however, far from optimal, which clearly confirms the urgent need for interventions to improve access to new innovative medicines throughout the region.

The goal of the care or therapy for every patient is to use the right medicine at the right time. In countries such as the UK or Germany, selected medicines may be available in the reimbursement system even immediately after registration, which means that patients may have immediate access to the selected latest treatments. In the UK, their utilization typically increases following a positive decision from NICE, which in the case of new medicines for cancer and rare diseases includes patient access programs. For some medicines, this means that the investment can be misguided, but this risk is borne by these countries as they prioritize patient access to therapeutic innovations (i.e. medicines that best fit the patient's characteristics and take into account scientific progress) until shown otherwise. In other countries, reimbursement decisions are made later, which means that patients potentially do not get the optimal therapeutic effect. However, this means that resources may be saved until the effectiveness and/ or safety of a new medicine has been demonstrated in routine clinical care especially if new medicines have only been studied on a limited number of patients before registration approval[19,20]. If reimbursement decisions are made long after registration, the loss of therapeutic benefit increases every month, which should be avoided. Similar effects for the patient population will be brought about

[18] *Ferrario A, Arāja D, Bochenek T, Čatić T, Dankó D, Dimitrova M, Fürst J, Greičiūtė-Kuprijanov I, Hoxha I, Jakupi A, Laidmäe E, Löblová O, Mardare I, Markovic-Pekovic V, Meshkov D, i in. (2017) The Implementation of Managed Entry Agreements in Central and Eastern Europe: Findings and Implications. PharmacoEconomics 35(12):1271–1285.*

[19] *Godman B, Hill A, Simoens S, Selke G, Selke Krulichová I, Zampirolli Dias C, Martin AP, Oortwijn W, Timoney A, Gustafsson LL, Voncina L, Kwon H-Y, Gulbinovic J, Gotham D, Wale J, i in. (2021) Potential approaches for the pricing of cancer medicines across Europe to enhance the sustainability of healthcare systems and the implications. Expert Rev. Pharmacoecon. Outcomes Res. 21(4):527–540.*

[20] *Pontes C, Zara C, Torrent-Farnell J, Obach M, Nadal C, Vella-Bonanno P, Ermisch M, Simoens S, Hauegen RC, Gulbinovic J, Timoney A, Martin AP, Mueller T, Nachtnebel A, Campbell S, i in. (2020) Time to Review Authorisation and Funding for New Cancer Medicines in Europe? Inferences from the Case of Olaratumab. Appl. Health Econ. Health Policy. 18(1):5–16.*

by reimbursement restrictions, i.e. narrowing of the reimbursement indications in relation to the registration indications - by reducing the number of patients who could obtain a therapeutic effect. However, this has to be assessed against lack of funding in other areas under opportunity cost considerations. Consequently, it is important to determine what proportion of patients in the target population benefit the most from new treatments where resources are an issue.

The above observations lead us to focus in this report on the analysis of the three most important indicators, which are:

- **time from drug registration/ indication to reimbursement,**
- **availability of medicines for reimbursement, taking reimbursement restrictions into account,**
- **proportion of patients treated with selected drugs that represent the greatest health need in selected diseases.**

In addition, we present the overall result of the GAP analysis both in terms of individual diseases, therapeutic areas and national dimension.

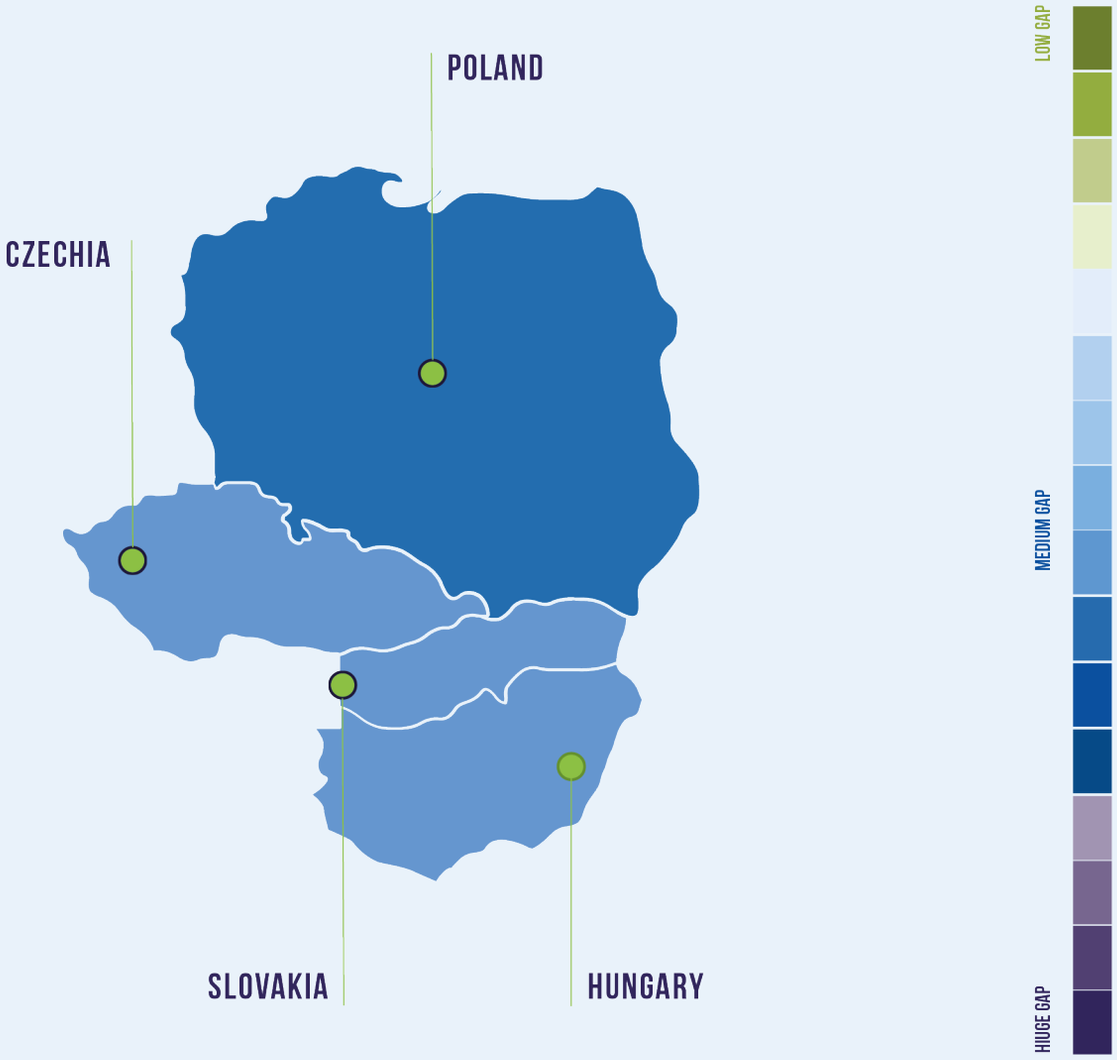
OVERALL GAP INDICATOR

The results of the main GAP indicator show appreciable limitations in access to new treatments for diagnosis and management in the 10 selected diseases. None of the countries scored above 50, which indicates a high-moderate limitation to therapeutic innovation. It should also be noted that there are large differences between the Visegrád Group countries since the difference between the best and the worst scores is almost 9 points (a relative difference of 23%). There are also appreciable reimbursement delays in each of the Visegrád Group countries with currently unsatisfactory scores in all of them with a large variation in individual therapeutic areas among the V4.

There are 2 main reasons for delays in regular systemic to new innovative treatments – late reimbursement application submission by pharmaceutical companies and the length of reimbursement process. Only approximately 50% of medicines recommended in clinical guidelines between 2010-2021 are available among the Visegrád Group countries. The most worrying findings for the Visegrád Group of countries comes from an indicator that shows what proportion of patients from the target population is treated with selected innovative medicines. The average value of this indicator barely exceeds 20% of the potential population for that treatment and. The main reason for this is the lack of regular reimbursement and the current protracted reimbursement processes. The main results are shown on the map, where the colours indicate the size of the GAP.

The highest GAP occurs in 2 KPIs: restrictions on reimbursement (KPI1) and share of patients on a specific novel treatment (KPI5).

Mean value of the top level aggregated indicator among Visegrád Group countries.



HOW TO READ THE SCALE?

The scale shows how big the GAP for a given country in the given area(s) and aspect(s) is. The scale is 0-100, where 100 indicates no restrictions for the given treatment or diagnosis and 0 represents lack of access to the preselected medicines or services. The results are presented as a color scale with best results (75 points and more) painted in green, worst results (25 points or less) painted in violet and the wide range of medium results presented in blue. With the exception of the green subscale, the darker shade relates to worse results.

The combined scores for a given country and disease generally are low to medium, which indicates an appreciable need for better treatment opportunities. In terms of the scale that means that the bars are painted mostly in blue, with the pale color indicating limited restrictions to the reference treatments or services and the deep blue representing substantial gaps in access to therapies.

CROSS-COUNTRY OVERVIEW

ORPHAN

The index at the level close to 38% indicates high GAP for all V4 countries.

CHRONIC DISEASES

The average GAP for the V4 countries is very moderate. The cumulative index reached the level of 46%.

ONCOLOGY

The average GAP for all V4 countries is moderate, close to 50% of the maximum achievable result.

TIME TO REIMBURSEMENT

The average time from registration to reimbursement for all included medicines was 940 days. This means that for such a long period of time patients could not be treated with the latest treatments. The average time between reimbursement and registration ranges from more than 2.1 years in Czechia to 3.4 years in Poland. These findings indicate that there is a significant delay in access to the latest innovations, which potentially translates into an appreciable burden on the population and indirectly into their life expectancy.

POLAND

Oncology 48

Orphans 34

Chronic Diseases 34

The most considerable GAPs in the health care access are in rare and chronic diseases.

SLOVAKIA

Oncology 47

Orphans 40

Chronic Diseases 50

The most considerable GAPs are in the access to the treatment and diagnostics in oncology and rare diseases.

CZECHIA

Oncology 53

Orphans 39

Chronic Diseases 57

The GAPs in treatment and diagnosis access are most significant in rare diseases.

HUNGARY

Oncology 52

Orphans 38

Chronic Diseases 43

The areas with the most significant GAPs in diagnosis and treatment access are both chronic and rare diseases.

CZECHIA

The longest reimbursement delay (expressed in days following the registration for the specific indication) was found for new treatments for lymphoma (3.9 years) and ovarian cancer (6.2 years). Reimbursement decisions are being made most rapidly for new treatments in AML, prostate cancer and multiple sclerosis (1.6-1.8 years) and SMA (0.5 year).

HUNGARY

The reimbursement delay (expressed in days between the reimbursement and the registration for specific indication) was the longest for new treatments for ovarian cancer and AML (no reimbursement yet) and cystic fibrosis (5.7 years). Conversely, the shortest time until a positive reimbursement decision was found for SMA (less than 1 year), diabetes (1.3 years), multiple sclerosis (3 years), and NSCLC (2.7 years).

POLAND

The time between registration for a specific indication and the reimbursement decision was the longest for new treatments for cystic fibrosis (7.4 years) and diabetes (5.2 years) and the shortest for NSCLC (2.3 years) and SMA (1.6 years).

SLOVAKIA

The longest reimbursement delay (expressed in days following the registration of the drug in a specific indication) was found for new treatments for cystic fibrosis (4.2 years) and some oncological medicines and indications, including ovarian cancer (6.3 years), prostate cancer (4.3 years), and breast cancer (5.1 years). The fastest reimbursement decisions were found in SMA (less than 1 year), multiple sclerosis (1 year), and AML (1.2 year).

SHARE OF PATIENTS ON A SPECIFIC NOVEL TREATMENT

The mean percentage of patients treated with selected drugs in each disease ranged from 0 to moderate values. Only in two diseases the percentage of patients treated with selected drugs exceeded 50% (ovarian cancer - Poland and Czechia; prostate cancer - Hungary, Czechia, Slovakia). In the remaining cases, the results can be described as very low and low. In cystic fibrosis and multiple sclerosis in 2020, no patient was treated with the selected medicines. The average value of this indicator is just over 20%, which means that only one fifth of patients are treated with the latest innovative medicines selected for this indicator.

CZECHIA

In Czechia the low proportion of patients treated with selected medicines in lymphoma and with PD-1/PD-L1 inhibitors in NSCLC is a considerable concern, as well as no patients treated with selected new medicines for cystic fibrosis and multiple sclerosis. However, there is a high proportion of patients treated with LAAs in diabetes in Czechia.

HUNGARY

In Hungary, there is a worryingly low proportion of patients that are currently being treated with PARP inhibitors in ovarian cancer and a rather low proportion of patients treated with LAAs in diabetes. No patients were treated with the use of selected drugs in cystic fibrosis, SMA and very low percentage of patients with AML were being treated new selected medicines. Hungary has a high proportion of patients treated with CDKI in breast cancer.

POLAND

In Poland a considerable concern are the lack of treatment with selected drugs in SMA, cystic fibrosis, multiple sclerosis and AML and the very low percentage of patients treated with LAAs in diabetes.

SLOVAKIA

In Slovakia, a considerable concern is the lack of treatment with selected drugs in SMA, cystic fibrosis and multiple sclerosis and the very low proportion of patients treated with PARP inhibitors in ovarian cancer and PD-1/PD-L1 inhibitors in NSCLC.

SHARE OF PATIENTS ON A SPECIFIC NOVEL TREATMENT

	BREAST CANCER	NSCLC	OVARIAN CANCER	PROSTATE CANCER	AML	LYMPHOMA	SMA	CYSTIC FIBROSIS	DIABETES MELLITUS	MULTIPLE SCLEROSIS
POLAND	23	22	51	46	0	27	0	0	11	0
HUNGARY	30	18	57	54	15	10	10	0	43	0
CZECHIA	14	4	1	55	17	47	0	0	32	0
SLOVAKIA	46	26	28	58	11	32	37	0	24	0

RESTRICTIONS ON REIMBURSED USE

This indicator aims to provide information on how many medicines are reimbursed taking into account reimbursement limitations (narrowing of populations). The results of this indicator are among the lowest of all analyzed indicators. The average value of this indicator is 25, which is equivalent to only one in four medicines being reimbursed for the whole authorized population. This indicator shows us in the clearest way what is the size of the current GAP.

CZECHIA

In Czechia, the greatest number of restrictions in access to novel treatment are in the rare diseases.

These results are driven mainly by the reimbursement restrictions as the number of technologies covered by the payer is limited in the following indications: AML (3 out of 9 authorized technologies reimbursed with some restrictions), SMA (1 out of 3 authorized technologies reimbursed in EAP) and cystic fibrosis (2 out of 9 authorized technologies reimbursed with some limitations). In two diseases (MS, CF) none of the medicines selected for detailed analysis were found to be reimbursed.

In oncology, reimbursement restrictions are particularly evident in ovarian cancer (1 out of 5 authorized technologies reimbursed with some restrictions).

POLAND

In Poland, the greatest number of restrictions in access to novel treatment can be observed in both rare and chronic diseases.

These results are driven mainly by the reimbursement restrictions as the number of technologies covered by the payer is highly limited in the following indications: AML (1 out of 9 authorized technologies reimbursed with some limitations), cystic fibrosis (2 out of 9 authorized technologies reimbursed with some limitations), SMA (1 reimbursed drug out of 3 authorized options) and diabetes (8 out of 36 authorized technologies reimbursed with some restrictions, no analyzed treatment was fully reimbursed).

Moreover, in four diseases (MS, SMA, CF, AML) none of the medicines selected for detailed analysis were found to be reimbursed in Poland.

In oncology, the reimbursement restrictions are particularly evident in prostate cancer (3 out of 8 authorized technologies reimbursed with restrictions).

HUNGARY

In Hungary, the greatest restrictions in access to novel treatment are observed in rare diseases.

These results are driven mainly by the reimbursement restrictions as the number of technologies covered by the payer is very

limited in these indications, and additionally, by an inadequate diagnostics quality.

Reimbursement is most limited in ovarian cancer (1 technology reimbursed in EAP out of 5 authorized options) and rare diseases, including AML (2 out of 9 authorized options reimbursed in the EAP) and lymphoma (3 drugs reimbursed out of 17 authorized technologies). In Hungary, there are two diseases (MS, CF) in which none of the novel drugs selected for detailed analysis are financed from the public funds.

SLOVAKIA

In Slovakia the greatest restrictions in access to novel treatment are in oncology and rare diseases.

These results are driven mainly by the reimbursement restrictions as the number of technologies covered by the payer is very limited in oncological indications, including ovarian cancer (1 out of 5 authorized technologies reimbursed with some restrictions), prostate cancer (3 out of 8 authorized technologies reimbursed, all with some restrictions), breast cancer (6 out of 14 authorized technologies reimbursed, all with restrictions), and rare diseases, including AML (4 out of 9 technologies reimbursed, all with some restrictions), SMA (1 out of 3 authorized technologies reimbursed with some restrictions), lymphoma (7 out of 17 authorized technologies reimbursed with some restrictions), and cystic fibrosis (1 out of 9 authorized technologies fully reimbursed, with additional 4 reimbursed with some restrictions).

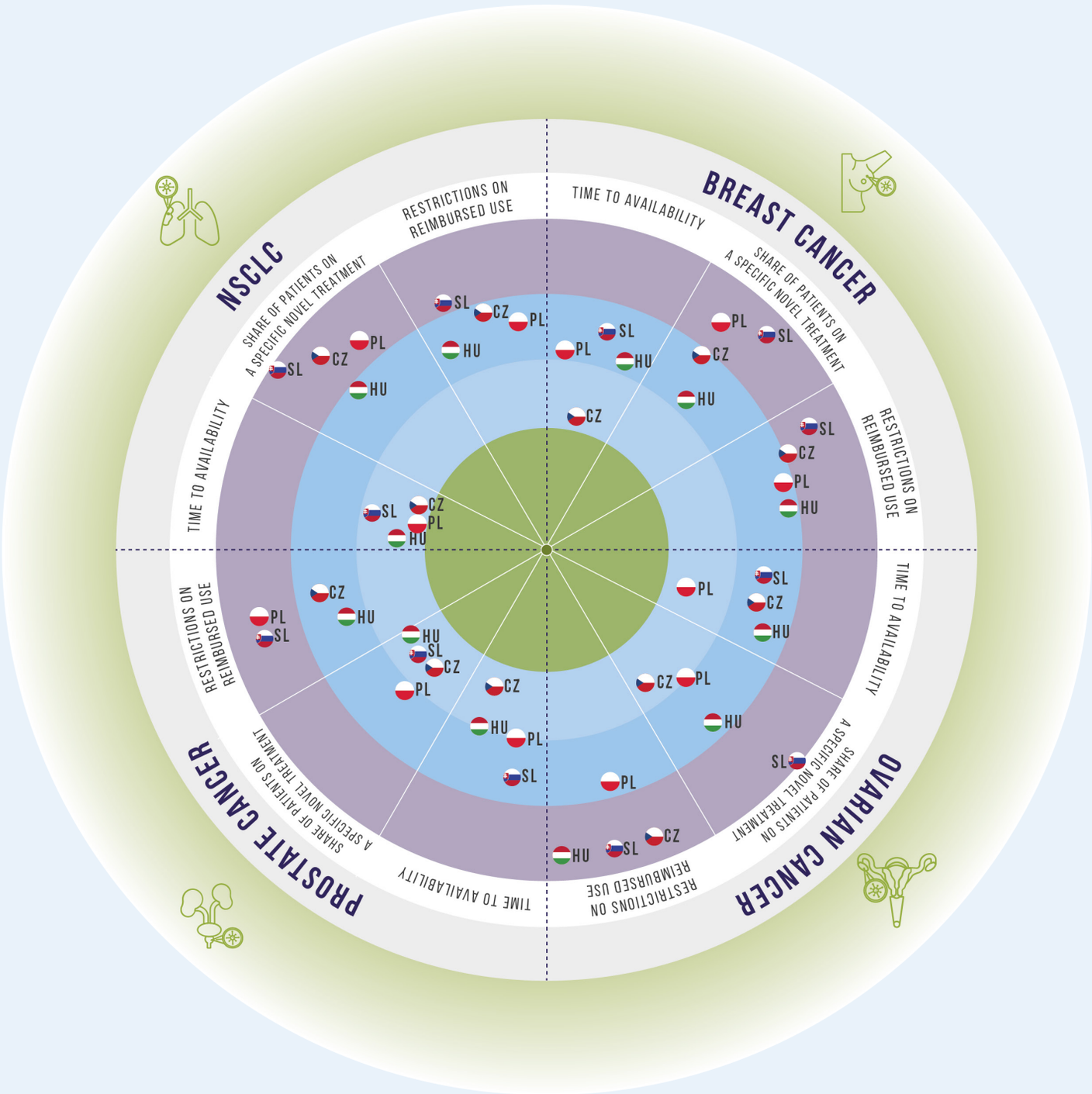
Moreover, there are three diseases (MS, CF, SMA) for which none of the novel medicines selected for detailed analysis are currently reimbursed. At the same time, in the following two areas (NSCLC, OC), the proportion of patients treated with the drugs is marginal (<5%).

TO SUM UP...

Where each country stands for the three indicators described earlier that are most relevant from a project perspective is summarized by the MAPs of the GAP. **The further a country is from the center of the circle, the larger the GAP is.**

ONCOLOGY

MAP OF THE GAP



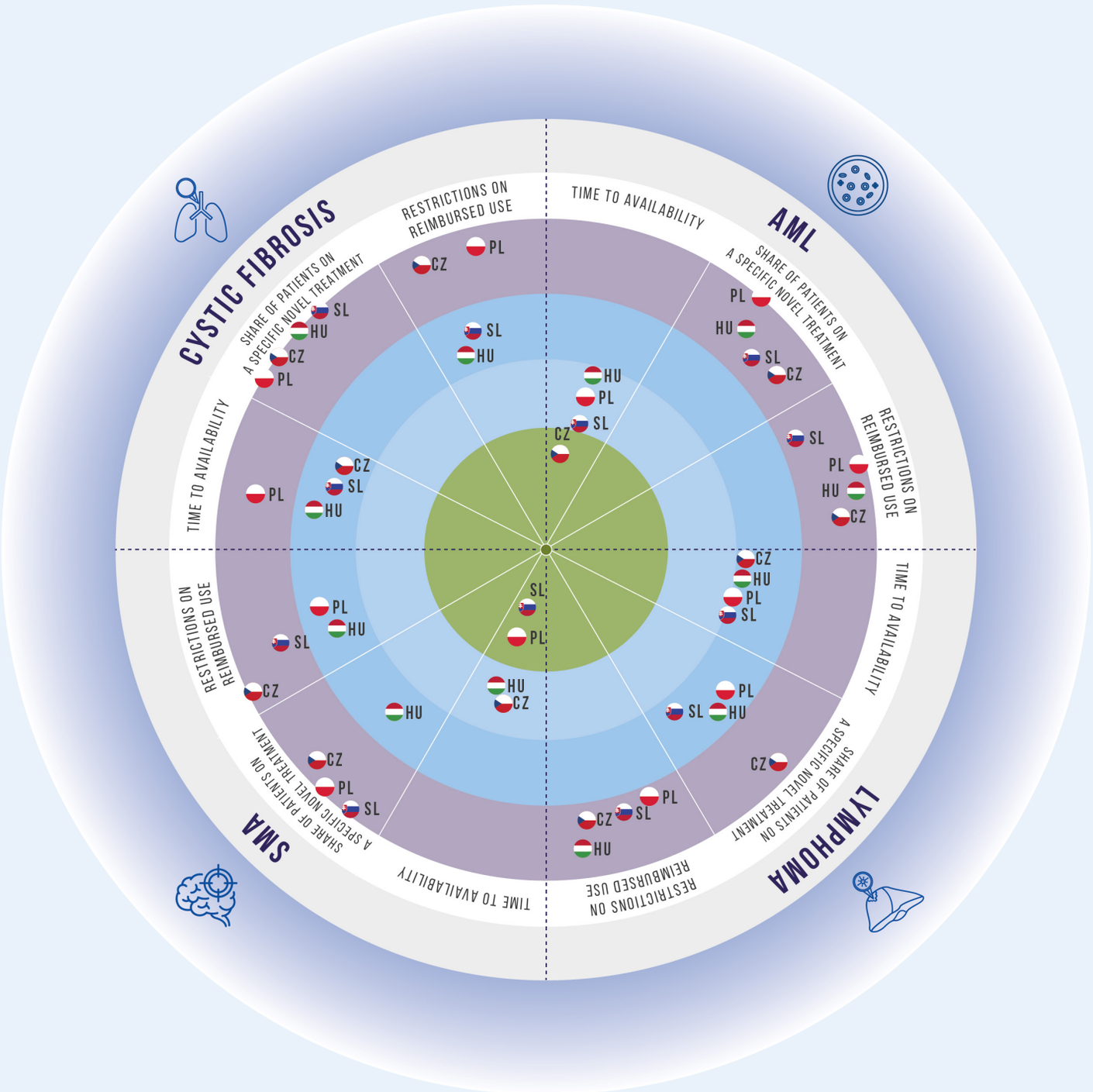
LEGEND

- POLAND
- HUNGARY
- CZECHIA
- SLOVAKIA

- LOW GAP
- MEDIUM GAP
- HUGE GAP

ORPHANS

MAP OF THE GAP



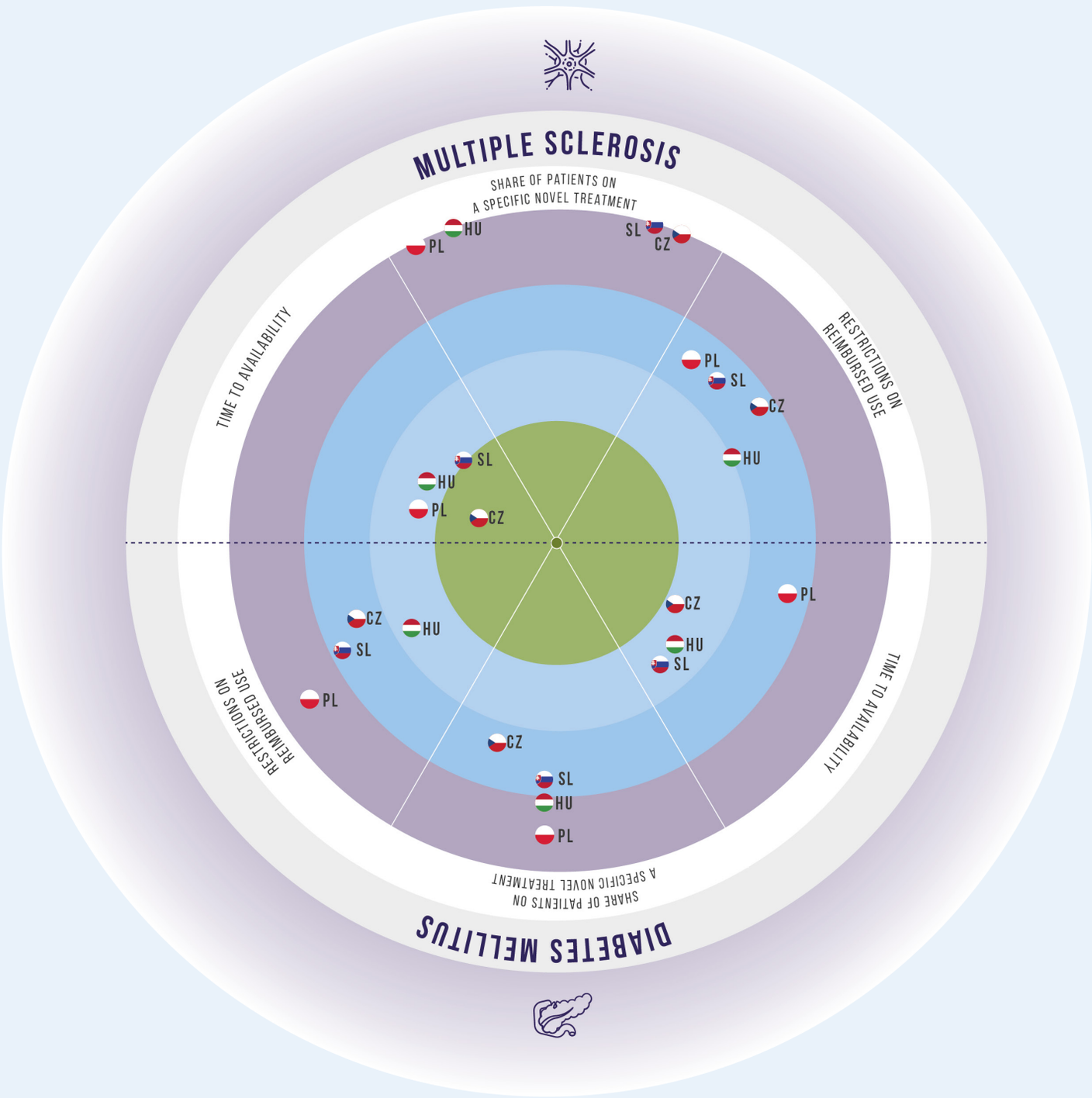
LEGEND

- POLAND
- HUNGARY
- CZECHIA
- SLOVAKIA

- LOW GAP
- MEDIUM GAP
- HUGE GAP

CHRONIC DISEASES

MAP OF THE GAP



LEGEND

- POLAND
- HUNGARY
- CZECHIA
- SLOVAKIA

- LOW GAP
- MEDIUM GAP
- HUGE GAP

REPORT CONCLUSION

THE GAP IN ACCESS TO THERAPIES IN V4 IS HIGH – IT'S TIME TO ACT.

The GAP project shows that both increasing the number of reimbursed therapies and eliminating criteria that narrow the access is a must. Our indicators confirmed that the time lag between drug registration and reimbursement shall be reduced, and access to diagnostics shall be improved in a significant manner. Challenges related to the reimbursement procedures and timely access to diagnostics are areas where joint action may be needed. We identified gaps and potential areas to improve further, thought we also stated that some of the recent national initiatives have some clearly visible outcomes. In Hungary our results show relative impressive coverage with orphans mainly due to the extensive early access programmes in the name the patient programme, and in Czech the high value score in time to availability dimension reflects to new and efficient pricing and reimbursement procedures.

The highest cumulative GAP for the Visegrád Group was identified for rare diseases in comparison to oncological or chronic diseases. The number of available medicines is limited in all the countries, especially in spinal muscular atrophy and cystic fibrosis. In rare oncological diseases, on the other hand, there is a much greater variation between individual Visegrád Group countries, indicating high inequalities in access to the latest medical technologies. The GAP results for the oncological treatment are better, however, differences between the Visegrád Group countries are still significant – especially in ovarian and prostate cancer. The highest dispersion in the GAP results across Visegrád Group countries is observed in chronic diseases. The time to access and the scope of available reimbursement options are uneven, particularly in diabetes mellitus.

In each of the analyzed diseases, at least major limitations in access to the latest therapeutic options as well as the rapid diagnosis were identified. On the example of these selected disease entities, it can be concluded that similar limitations exist in other diseases. This means that patients in Visegrád Group countries are not treated in the most optimal way as indicated in clinical guidelines. This contributes to suboptimal health outcomes, increased DALY burden, and increased indirect costs.