ARWeN

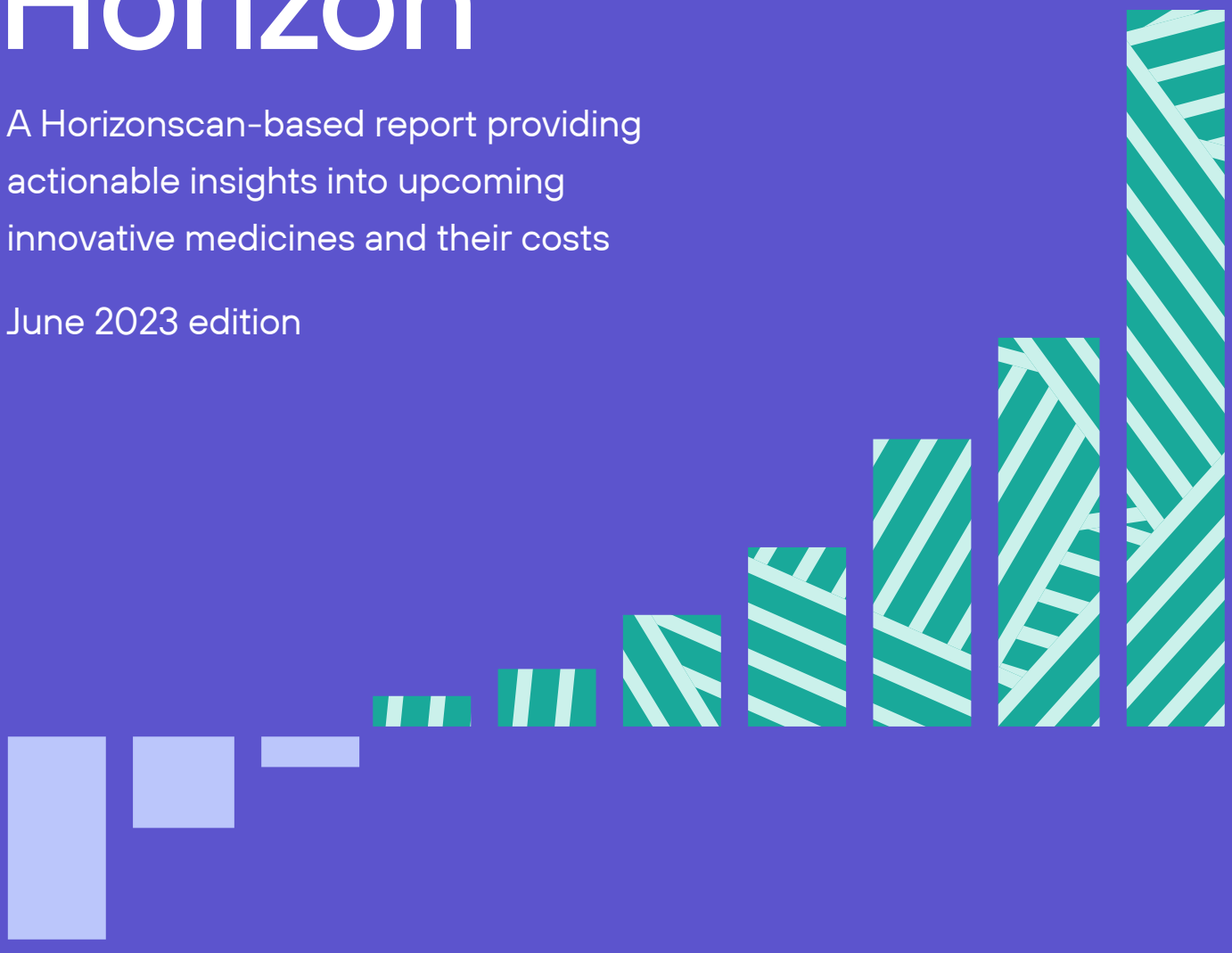
Actionable Real-World Evidence Network

Powered by LOGEX

On the Horizon

A Horizonscan-based report providing actionable insights into upcoming innovative medicines and their costs

June 2023 edition



Key insights

- For the next two years, most new medicines are expected in the fields of oncology, hematology and neurology
- Eye disorders like AMD and DME, as well as certain infectious diseases, are rapidly gaining interest from the pharmaceutical industry over the last years
- Orphan drugs are on the rise; over the last year, a 17% increase in the number of orphan drugs has been observed, most of which are in the neurology domain
- Lung cancer medicines will have the biggest impact on hospital budgets due to both high-cost drugs being administered already and new expensive treatments coming up
- Over the last years, the rate of growth for new medicines was highest in the field of infectious diseases
- By deciding not to include sacituzumab govitecan, a breast cancer medicine manufactured by Gilead, in the reimbursed basic care package, the Ministry of Health, Welfare and Sport has effectively saved an estimated per-hospital budget impact of €2.9 million.

Horizonscan medicines

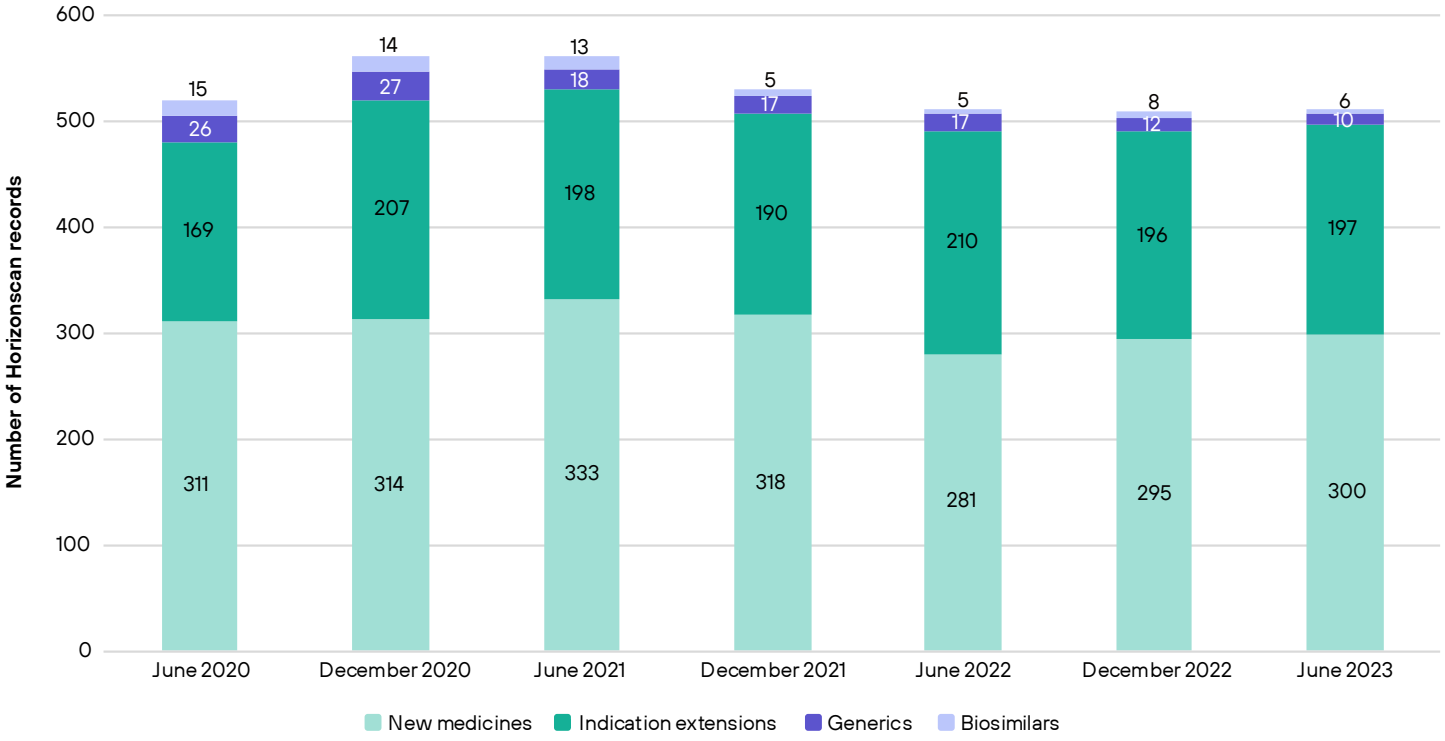
The National Health Care Institute (NHCI) issued the 12th edition of the Horizonscan medicines database on June 6, 2023[1]. Since 2018, the Horizonscan has been providing an accessible and comprehensive overview of medications projected to become available in the Dutch market within the next two years. This database encompasses various types of medications, including novel proprietary drugs, extensions of indications for existing drugs, generics, and biosimilars. Detailed information regarding their mechanism of action, anticipated patient volume, treatment efficacy, registration dates, and financial impact is included. Such data is instrumental in initiating processes related to the inclusion of medications in basic healthcare packages or engaging in pre-registration compensation negotiations. Furthermore, the Horizonscan serves as an early-stage source of information for patients, healthcare professionals, hospitals, health insurers, and government entities, enabling them to stay abreast of advancements in the realm of innovative medications. Given the constantly evolving pharmaceutical industry landscape, staying informed about newly introduced medications can be challenging. The Horizonscan serves as a valuable tool for healthcare stakeholders, enabling them to navigate this dynamic environment with ease.

The present edition of the On the Horizon report sheds light on the Horizonscan publications spanning the last three years, encompassing a total of seven releases. The report delves into various aspects, including the number of new medications categorized by disease domain, the annual financial impact per hospital resulting from the costliest forthcoming medications, and an examination of pharmaceutical interest in specific disease areas. Additionally, special attention has been given to the upward trend observed in the development of orphan drugs. The report addresses the expected number of orphan drugs entering the market, prevalent indications for orphan drug development, and the disease area that has experienced the most substantial growth in the past year. Detailed insights on these topics can be found in the current edition of On the Horizon.

The number and type of horizonscan records remains unchanged

The latest iteration of the Horizonscan encompasses a total of 513 documented drugs (Figure 1), representing a consistent count compared to the two preceding editions. Within the compilation, the majority share is attributed to newly introduced medications, comprising 58% of the total, followed by indication extensions (38%), generics (2%), and biosimilars (2%). From June 2020 to now, we see a decrease in the proportion of biosimilars (from 3% to 1%) and generics (from 5% to 2%) of the total number of records included. The decline in generics and biosimilars could adversely affect access to affordable treatments and lead to higher healthcare expenses. It emphasizes the importance of vigilant monitoring, strategic planning, and prioritizing patient access to essential medications to ensure sustainable healthcare systems and the availability of cost-effective options.

Fig. 1: **Total number of Horizonscan records by type of medicines over time**



Eye disorders in the top 3 of most drugs included

In recent years, the top 10 indications expected to receive the most new medicines and indication extensions have shown a generally consistent trend, although there have been significant changes in the most recent edition (Figure 2). Lung cancer consistently emerges as an area experiencing continuous growth, ranking first on the list with an expected influx of 33 new medicines and indication extensions in the upcoming years. Moreover, there has been a significant surge in the development of medications targeting eye disorders such as age-related macular degeneration (AMD) and diabetic macular edema (DME), resulting in a notable ascent of four positions and currently securing the third rank in terms of the anticipated number of medicines in the current edition. Furthermore, there has been a discernible increase in the development of drugs combating bacterial infections, likely associated with the heightened attention surrounding infectious diseases in the post-COVID era.

Additionally, it is worth mentioning that the number of medicines specifically aimed at addressing COVID-19 has notably diminished, causing a shift in its ranking from the 10th position to the 13th. The current edition includes only nine newly developed COVID-19 medicines, in contrast to the 14 medicines documented in the previous year. As the COVID-19 pandemic has subsided, pharmaceutical industry interest in this domain has markedly declined.

Fig. 2: **The top 10 indications with the highest expected number of new medicines and indication extensions**

Rank	June 2020	Records
1	**Skin diseases**	22
2	**Lung cancer**	19
3	**Bacterial infections**	19
4	Metabolic diseases	18
5	Diabetes	18
6	**Breast cancer**	17
7	**Multiple Myeloma**	16
8	Stem cell transplants	16
9	Eye disorders	14
10	AML / MDS	13

Rank	December 2020	Records
+1	**Lung cancer**	28
+4	**Breast cancer**	22
	Bacterial infections	21
-3	**Skin diseases**	20
+2	**Multiple Myeloma**	20
-1	Diabetes	18
-3	Metabolic diseases	17
+1	Eye disorders	15
-1	Stem cell transplants	13
	AML / MDS	12

Rank	June 2021	Records
	Lung cancer	25
+2	**Skin diseases**	21
-1	**Breast cancer**	20
-1	**Bacterial infections**	19
	Multiple Myeloma	19
+1	Metabolic diseases	18
+1	Eye disorders	15
-2	Diabetes	12
	Stem cell transplants	11
	AML / MDS	11

Rank	December 2021	Records
+5	Metabolic diseases	29
-1	**Lung cancer**	28
-1	**Skin diseases**	19
-1	**Breast cancer**	19
	Multiple Myeloma	18
-2	**Bacterial infections**	14
	Eye disorders	13
+4	Prostate cancer	13
+60	COVID-19	12
-2	Diabetes	11

Rank	June 2022	Records
+1	**Lung cancer**	33
-1	Metabolic diseases	23
+2	**Multiple Myeloma**	20
-1	**Skin diseases**	18
-1	**Breast cancer**	17
+3	COVID-19	14
	Eye disorders	13
	Prostate cancer	11
+2	**NHL**	11
-4	**Bacterial infections**	10

Rank	December 2022	Records
	Lung cancer	33
	Metabolic diseases	25
	Multiple Myeloma	17
+5	**NHL**	16
	Breast cancer	16
-2	**Skin diseases**	16
	Eye disorders	12
+1	Diabetes	12
-1	Prostate cancer	11
-4	COVID-19	11

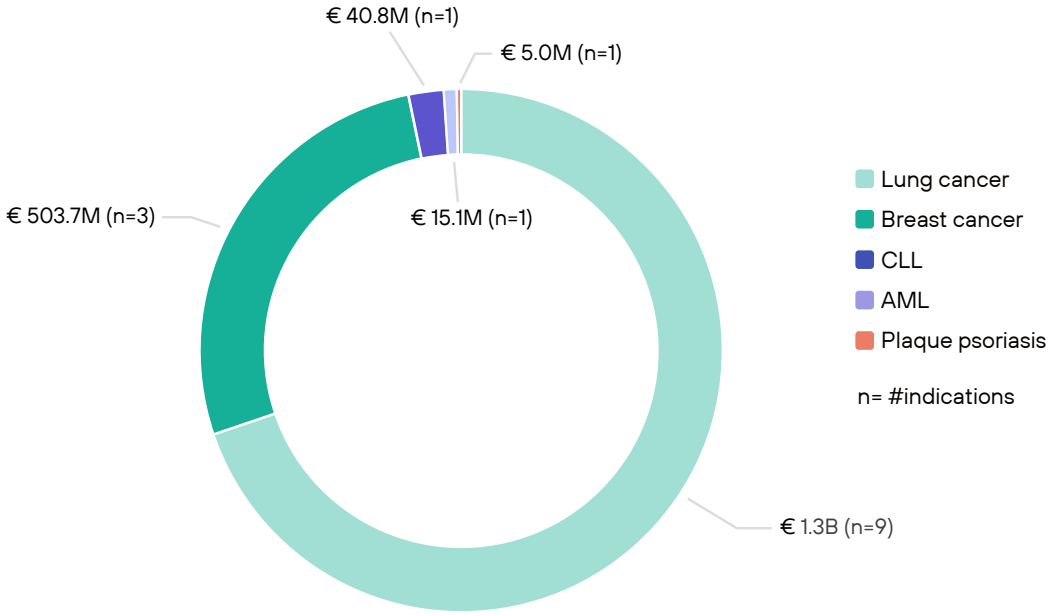
Rank	June 2023	Records
	Lung cancer	33
	Metabolic diseases	25
+4	Eye disorders	17
+2	**Skin diseases**	16
	Breast cancer	16
-3	**Multiple Myeloma**	16
-3	**NHL**	12
+4	**Bacterial infections**	12
-1	Diabetes	11
-4	Prostate cancer	11

The annual budget-impact of the 10 most expensive drugs

In our recent analysis, we conducted an assessment of the annual financial impact associated with the top 10 most costly medications within the ARWEN focus disease domains. These domains encompass lung cancer, breast cancer, acute myeloid leukemia (AML), chronic lymphocytic/myeloid leukemia (CLL/CML), as well as skin diseases like atopic dermatitis and psoriasis. The medications under consideration are projected to undergo registration in the Netherlands between June 2023 and June 2025. According to the latest data from the Horizonscan, these medications are anticipated to incur a total annual cost of €1.87 billion*. Among the ARWEN (the Actionable Real World Evidence Network of LOGEX) focus disease areas, lung cancer represents the highest expected expenditure, amounting to €1.3 billion, encompassing nine distinct indications (Figure 3).

Fig 3: **Total expected annual healthcare costs of the most expensive medicines with registrations in the coming 2 years**

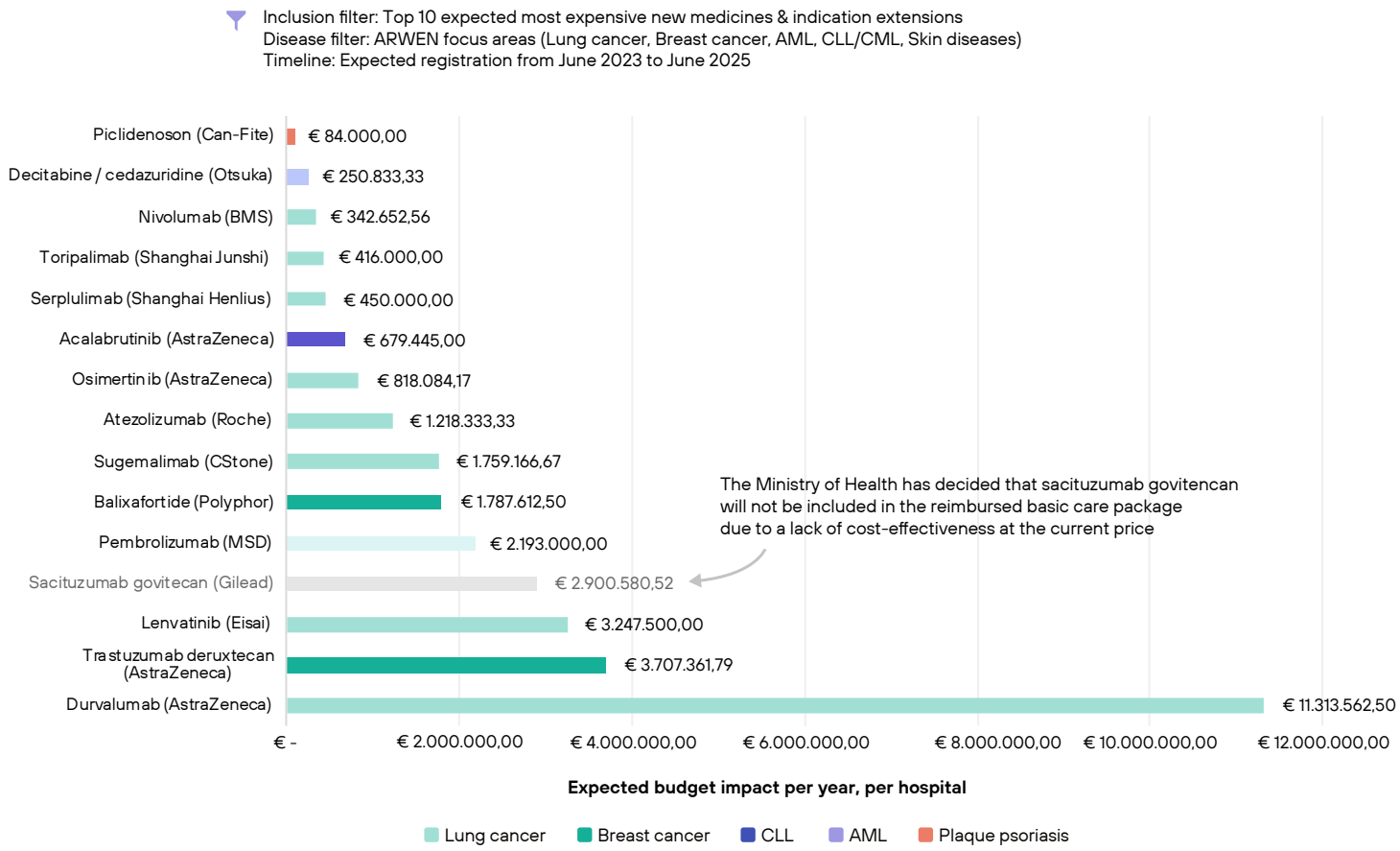
Inclusion filter: Top 10 expected most expensive new medicines & indication extensions
Disease filter: ARWEN focus areas (Lung cancer, Breast cancer, AML, CLL/CML, Skin diseases)
Timeline: Expected registration from June 2023 to June 2025



Presented below is an overview of the projected annual budget impact per hospital for the anticipated medicine costs, offering hospitals insight into the scale of forthcoming medications (see Figure 4). Notably, the fourth most expensive medication, sacituzumab govitecan, has recently been denied inclusion in the reimbursed basic care package in the Netherlands due to insufficient evidence supporting its cost-effectiveness[2]. The breast cancer medicine, marketed globally under the brand name TRODELVY by Gilead, demanded a price deemed "disproportionate" to the health benefits it provides.

* This number is based on the predicted eligible patient volumes and cost per patient per year as described in the Horizonscan for each medicine. It should be noted here that the real-world uptake and correlated total healthcare expenditure for these medicines may deviate significantly, for example due to medicines being retracted from the application process, competition of other medicines, disappointing real-world outcomes, personal medical preferences or strategic decision-making by healthcare institutions.

Fig 4: **Expected annual hospital budget impact of the most expensive drugs with registrations in the coming 2 years**



In response, Ernst Kuipers, Minister of the Ministry of Health, Welfare and Sport, has demanded a 75% discount on the proposed price by Gilead before considering the inclusion of the medication in the basic care package. The individual hospital budget impact of the medicine was estimated at €2.9 million**.

Minister Kuipers remarked:

> "I would have preferred the supplier to agree to a socially acceptable price so that the product could be incorporated into the basic package. Unfortunately, that did not transpire. The predicament lies in the fact that while this medication does generate health gains, those gains do not align proportionally with the requested price, thereby negating its effectiveness in providing care. Inefficient spending on a drug means reduced funding for other vital areas of care. That is not the direction I wish to pursue."

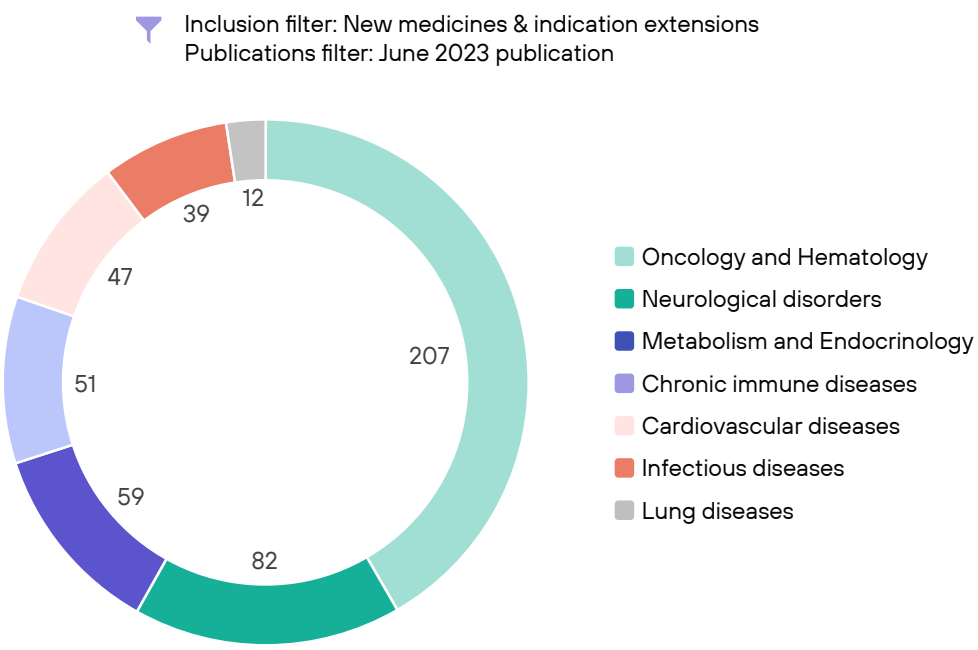
Healthcare expenditure is increasing at a rapid pace. To ensure solidarity within our reimbursement system both now and in the future, it is imperative to curtail drug prices and expenditure. Consequently, it is possible for a medication to offer health benefits, but those benefits may not align proportionately with the associated price, thereby compromising its effectiveness in delivering care. The recently concluded comprehensive care agreement (Integraal Zorgakkoord) [3] underscores the necessity of making prudent decisions regarding the allocation of our collective financial resources.

** Per-hospital yearly budget-impact is calculated by dividing the total expected yearly healthcare cost of a top 10 high-expensive medicine by 60, since we expect that on average, around 60 hospitals in The Netherlands will prescribe these medicines.

Many new medicines in the oncology & neurology pipelines

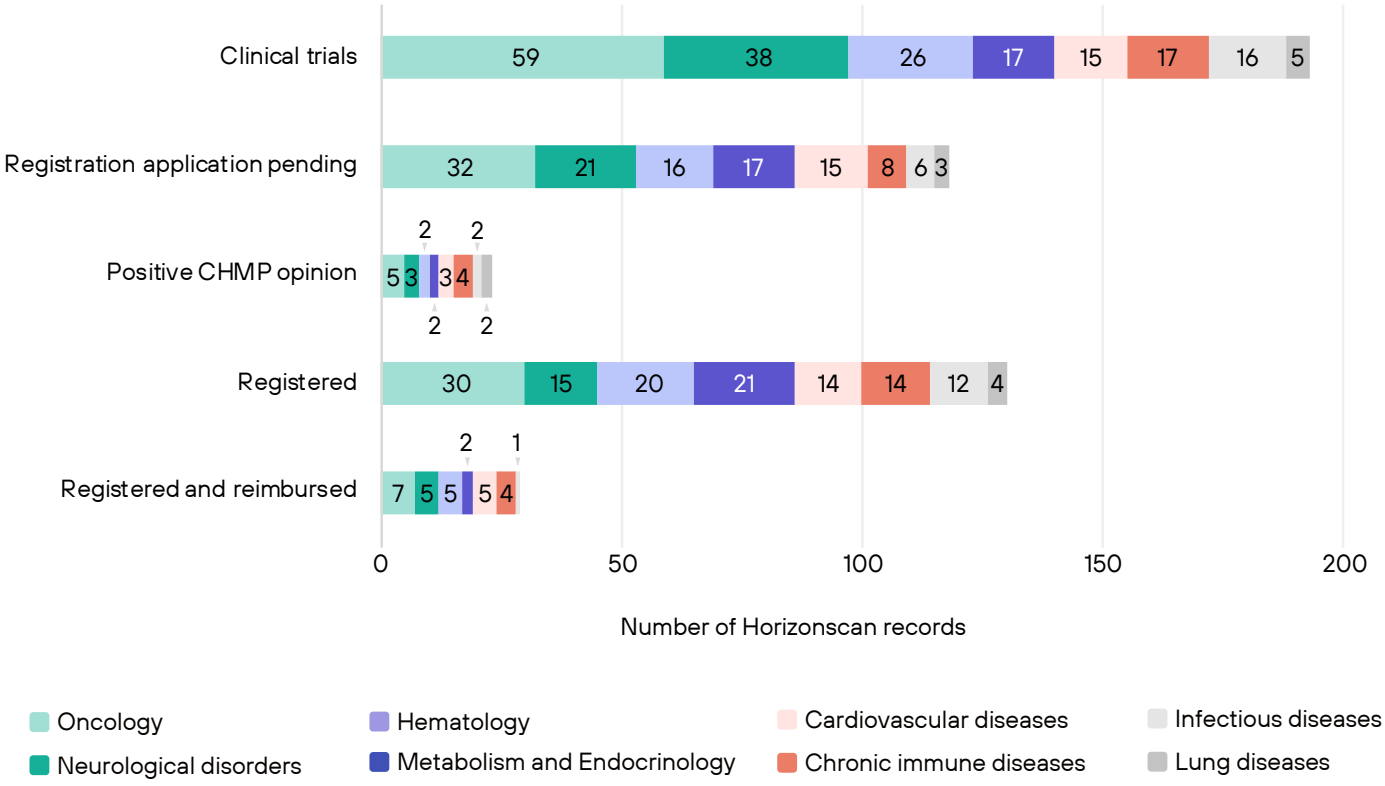
In terms of overall distribution, the majority of medications included in the Horizonscan database target oncological, hematological, and neurological diseases (Figure 5). These domains encompass conditions like lung cancer, breast cancer, multiple myeloma, as well as neurological disorders affecting the eyes and muscles, such as age-related macular degeneration (AMD), diabetic macular edema (DME), and generalized myasthenia. This trend has demonstrated relative stability over the years, with limited fluctuations in the composition of these therapeutic domains.

Fig 5: **Horizonscan records by disease domain**



Upon further analysis of the medicines' distribution based on their lifecycle phases, it becomes apparent that a substantial portion of the medications featured in the Horizonscan is in the clinical trial phase. Within this subset, again, a significant emphasis is placed on oncological and hematological diseases (Figure 6).

Fig 6: **Horizonscan records by disease domain per lifecycle phase**

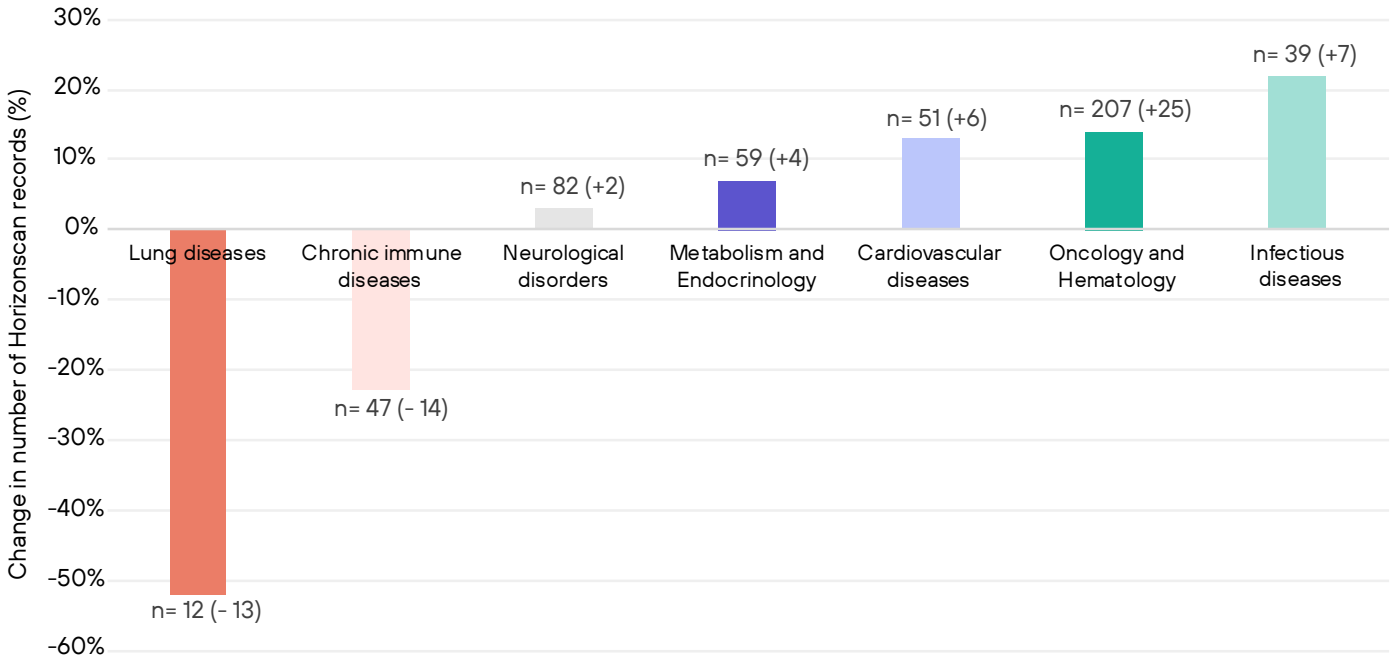


In terms of changes observed in the number of included medicines per domain over the past three years, notable reductions have been witnessed in the domains of lung diseases and chronic immune diseases. Specifically, there has been a significant decline of 52% and 23% respectively (Figure 7). This decline holds considerable significance, potentially attributable to the intricate and heterogeneous nature of lung and chronic immune diseases. The complexity involved in comprehending their underlying mechanisms and developing effective treatments presents considerable challenges. Moreover, the development of novel medicines for chronic immune diseases may face obstacles due to safety concerns associated with existing medications like JAK inhibitors[4]. Reports of severe side effects, including increased risks of infections, blood clotting, and malignancies, have raised cautionary flags. Consequently, pharmaceutical companies encounter hurdles in innovating safer alternatives, thereby impeding progress in expanding therapeutic options for patients with chronic immune diseases.

Infectious diseases account for the biggest increase in new medicines

Interestingly, certain disease domains have experienced rapid growth in terms of the inclusion of new medicines in the Horizonscan. Cardiology and infectious diseases stand out in this regard. Over the years, there has been a discernible increase in the development of medicines targeting diseases such as atrial fibrillation and bacterial infections. As explored in the previous edition of On the Horizon[5], the surge in medicines for infectious diseases can be largely attributed to the impact of the COVID-19 pandemic, which significantly boosted the registration of medications in this domain. When we look at the growth in neurology medicines, we don't see a big increase over the last 3 years. However, what is worth mentioning here is that over the last year, the number of neurology medicines has grown by 15%, from 71 to 82 medicines included.

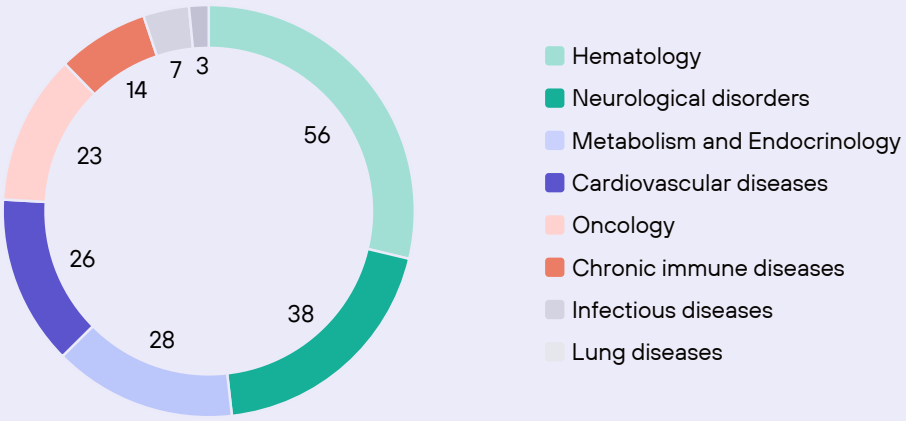
Fig 7: **Change in number of Horizonscan records per disease domain over time**



Deep dive: The rapid rise of orphan drugs

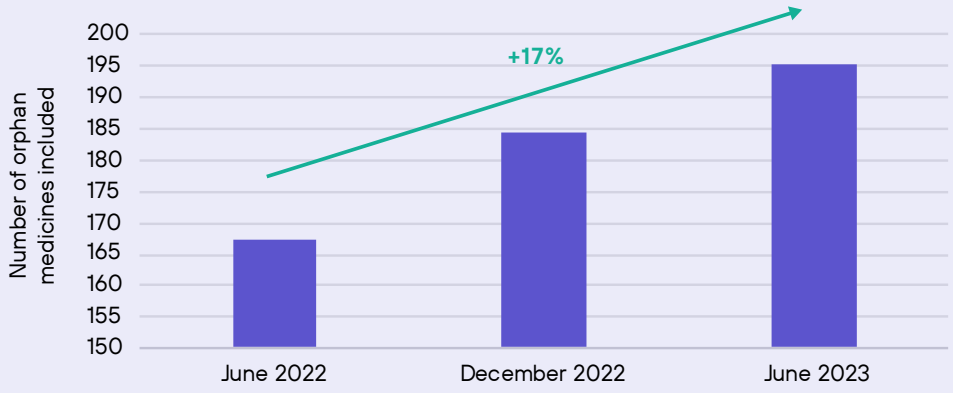
In this deep dive, we will take a look at the rapid rise of orphan drugs over the last years. Orphan drugs are generally known as medications developed to treat rare diseases that affect a small population of patients. The development of orphan drugs is crucial as it addresses the unmet medical needs of rare diseases, providing hope and improved quality of life for patients who would otherwise have limited or no treatment options. Judging by the latest Horizonscan, most orphan drugs today are being developed for hematological, neurological and endocrinological diseases such as non-Hodgkin's lymphoma, Huntington's disease, and Hunter syndrome (Figure 8).

Fig 8: **Orphan drugs included in Horizonscan June 2023 by disease domain**



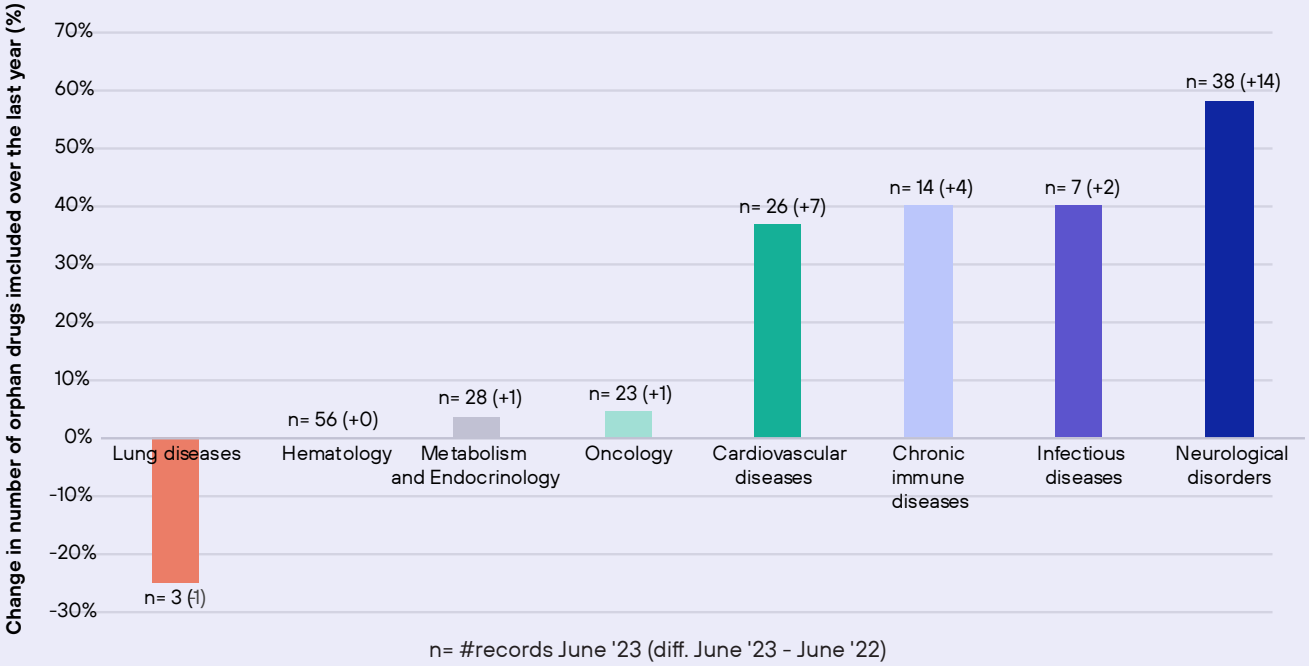
Over the last year, we have observed a rapid 17% rise in the number of orphan drugs included in the Horizonscan (Figure 9), from 167 to 195 orphan medicines included, which may be considered a promising step towards addressing the unmet needs of individuals with rare diseases. It should be noted, however, that typically, a significant proportion of these orphan drugs will drop out during the development process and never reach the patient

Fig 9: **Number of orphan drugs included in Horizonscans over the last year**



Zooming in on the disease domains in which the number of orphan drugs has increased the most, we see that a growing number of orphan drugs is being developed for the treatment of cardiovascular-, immunological-, infectious-, and above all neurological diseases (Figure 11). Within the domain of neurology, the number of orphan drugs has increased by a shocking 58%, going from 24 to 38 orphan drugs included over the span of a year. One plausible explanation for the increasing development of orphan drugs for neurological disorders could be the growing understanding of the complex mechanisms underlying these disorders, advancements in neuroscience research, and the recognition of the significant burden they impose on patients and society, driving the need for innovative treatments and targeted interventions.

Fig 10: **Change in the number of orphan drugs included in Horizonscans over the last year (Horizonscan June 2022 - June 2023) per disease domain**



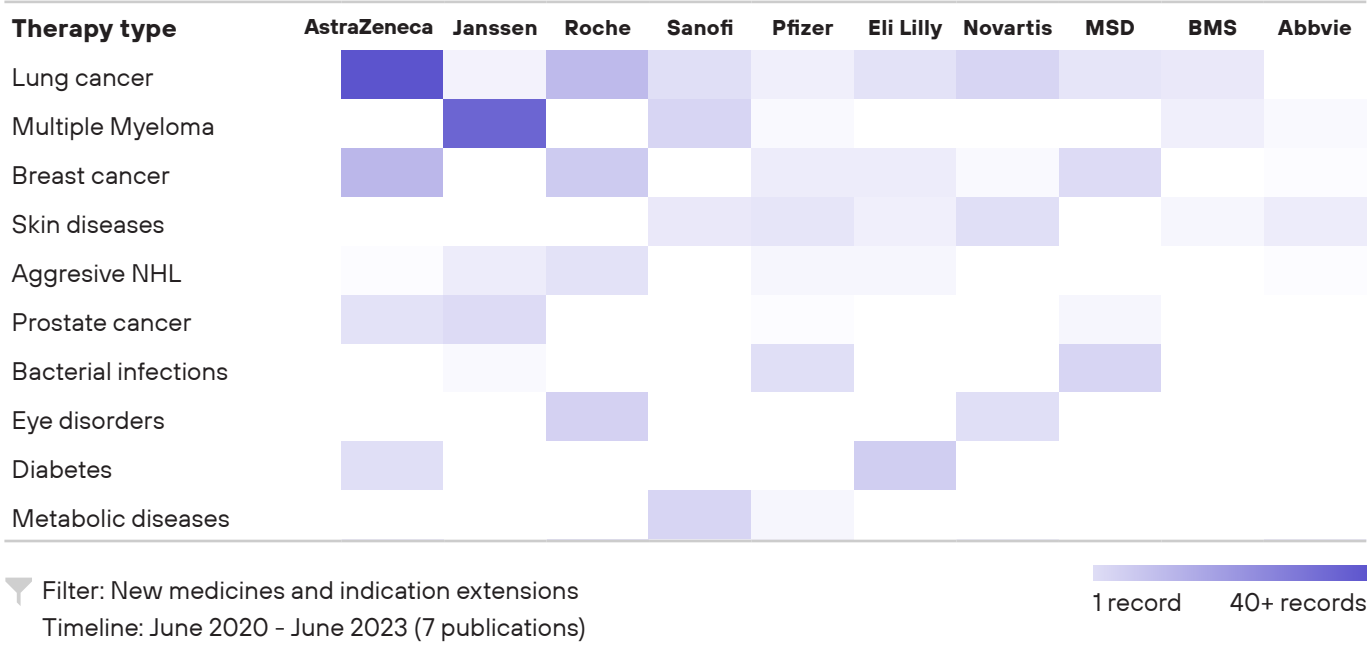
n= #records June '23 (diff. June '23 - June '22)

While the development of orphan drugs is on the rise, patient access to these crucial treatments often lags behind[6]. This delay stems from the lengthy process between the registration of an orphan drug and its inclusion in the reimbursed basic care package. As a result, patients with rare diseases may face significant challenges in obtaining these medications in a timely manner. A solution involves streamlining the registration and reimbursement processes, fostering collaboration among stakeholders, and exploring innovative pricing models to ensure timely and equitable access to orphan drugs while maintaining affordability and sustainability. The Orphan Drug Access Protocol is a good example of such a collaboration[7].

Mapping the interest of pharma in different disease areas

To provide a comprehensive overview of the top 10 indications with the highest number of new medications and indication extensions from pharmaceutical companies over the past three years, we have generated a heatmap (Figure 12). The heatmap illuminates the notable presence of AstraZeneca and Roche in oncological indications, specifically lung and breast cancer, as evidenced by the substantial introduction of new medications in these areas across each Horizonscan publication. Janssen also garners attention for its focus on multiple myeloma, while it is noteworthy that no breast cancer medications from Janssen have been mentioned in recent Horizonscan editions. Gilead, on the other hand, exhibits an intriguing portfolio concentration, diverging from the prevailing trend of lung cancer and other popular medical domains. Instead, Gilead's focus lies on relatively less competitive disease areas, such as non-Hodgkin's lymphoma and medications related to COVID-19.

Fig. 11: **Overview of the most frequently included therapy types in the Horizonscan per manufacturer**



Unlocking insights into the use of medicines with real-world evidence

The insights presented in this report are derived exclusively from the publicly accessible Horizonscan. However, it is worth noting that we have previously demonstrated the potential value of incorporating real-world data into this database[8]. Real-world data refers to information collected as part of routine clinical practice, such as claims and prescription data, and can provide valuable insights into patient volume and the budget impact that may differ from the expected figures in the Horizonscan. At LOGEX Life Sciences, our Actionable Real World Evidence Network (ARWEN) has been established to leverage such real-world data.

There are several areas in horizonscanning where the integration of real-world data holds promise, including:

1. Monitoring the uptake of innovative and expensive medicines, such as CAR-T therapies.
2. Evaluating the real-world cost-effectiveness of medicines previously included in the Dutch lock system[8].
3. Assessing the impact of innovative therapies on the standard of care over time, examining changes in treatment pathways, outcomes, and costs.
4. Providing healthcare providers with insights into the effectiveness and appropriate use of medicines in clinical practice, with the aim of complementing traditional clinical guidelines with real-world guidelines in the future.

Through ARWEN, we address these evidence gaps on a daily basis, serving multiple stakeholders in the healthcare sector. Our primary focus lies in generating real-world evidence during the peri-launch phase, spanning from market access and pricing to drug commercialization. We collaborate with and/or are commissioned by hospitals, researchers, governments, and pharmaceutical/MedTech companies.

To provide a glimpse into the range of insights we can offer within ARWEN, for any condition treated in a hospital setting, we can provide the following:

- **Drug use & epidemiology analyses**, answering questions like how many patients suffer from a certain disease; how many patients would be eligible for a certain drug; and how does that differ between countries?
- **Standard of care & patient pathway analyses**, answering questions like how and where in the patient pathway is a certain drug used in clinical practice; by which patient (sub)groups; and at which dose levels?
- **Therapy impact analyses on outcomes & costs**, answering questions like what is the impact of a (new) drug on the hospital or societal budget; What is the impact of a (new) drug on the outcomes of patients, for example, measured by Clinically Reported Outcomes Measures (CROMs) or Patient Reported Outcomes Measures (PROMs); or combining the aforementioned questions into a cost-effectiveness study or project around a certain (new) drug.

In addition to these study types, we also conduct market sizing and budget impact analyses during the drug discovery phase, identify target cohorts and optimize trials in the compound R&D phase, demonstrate value and engage with key opinion leaders in the regulatory approval phase, and conduct post-authorization safety and guideline adherence studies. Through our recent collaboration agreement[9] with P95, we are increasingly involved in real-world evidence projects in the field of infectious diseases, such as evaluating the cost-effectiveness of vaccines for specific diseases.

Way forward

In this report, we have presented a comprehensive overview of the anticipated number and cost of pharmaceuticals expected to enter the Dutch market in the coming years. Our analysis encompasses projected registrations within specific disease categories, trends in the pharmaceutical industry's focus over time, and a detailed examination of the rapid growth of orphan drugs within specific disease areas. These insights hold value for various stakeholders, including hospital pharmacies and health insurers, as they anticipate and adapt to changes in the medication landscape and evaluate budget implications.

As previously mentioned, we strongly believe in the potential of real-world evidence to inform decision-making and enhance access to innovative treatments. Real-world evidence can play a crucial role in monitoring health outcomes and cost benefits, as well as contributing to the development of real-world and real-time guidelines alongside traditional clinical guidelines. If you are interested in leveraging real-world data to improve healthcare or would like more information about our diverse projects throughout Europe, we invite you to contact us at www.arwen.eu to explore potential collaborations.

About the authors

Mart Schoondermark is a Business Developer in the LOGEX Life Sciences team. Jan van der Eijk is the Principal of Life Sciences at LOGEX.

Both authors are based in the Amsterdam office.

For questions or inquiries, please contact mart.schoondermark@logex.com or visit www.arwen.eu.

About LOGEX

ARWEN is part of LOGEX. With more than 450 dedicated colleagues, LOGEX helps more than 700 hospitals and thousands of healthcare professionals across Europe to turn their financial, operational and outcome data (clinical data and patient-reported data) into better care. Find more information about LOGEX's solutions here.

References

1. https://www.horizonscangeneesmiddelen.nl/geneesmiddelen
2. https://www.forbes.com/sites/joshuacohen/2023/05/01/dutch-ministry-of-health-will-not-reimburse-gileads-breast-cancer-drug-trodelvy/
3. https://www.rijksoverheid.nl/onderwerpen/kwaliteit-van-de-zorg/integraal-zorgakkoord
4. https://www.ema.europa.eu/en/news/ema-recommends-measures-minimise-risk-serious-side-effects-janus-kinase-inhibitors-chronic
5. https://arwen.eu/insights/report-on-the-horizon-actionable-insights-into-innovative-medicines-and-their-costs/
6. https://www.verenigninginnovatievegeneesmiddelen.nl/actueel/farma-facts-toegang-weesgeneesmiddelen-nederland-op-laag-niveau
7. https://medicijnvoordemaatschappij.nl/odap-orphan-drug-access-protocol/
8. https://www.zorginstituutnederland.nl/over-ons/programmas-en-samenwerkingsverbanden/horizonscan-geneesmiddelen/sluis-voor-dure-geneesmiddelen
9. https://p-95.com/logex-and-p95-to-jointly-build-the-international-infectious-disease-observatory-arwen-id/