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Actionable Real-World Evidence Network

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On the Horizon

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

March 2024 edition

Key insights

- Over the next two years, the majority of new medicines are anticipated to emerge in the areas of oncology, hematology, and neurology.
- Eye disorders such as Age-related Macular Degeneration (AMD) and Diabetic Macular Edema (DME) are contributing substantially to the rise in annual healthcare expenses. This increase is primarily attributed to the recent advancements in targeted treatments, which have the potential to extend the intervals between required injections, providing important patient- and healthcare resource utilisation benefits.
- Alzheimer's medications are expected to have the biggest effect on hospital budgets. This is due to two new and expensive treatments on the horizon, adding up to over one billion euros in total costs.
- Significant healthcare expenditures are anticipated for treatments designed for Non-Alcoholic Fatty Liver Disease (NAFLD), with several drugs in the pipeline poised for introduction.
- The field of lung cancer is expected to experience a notable increase in the introduction of new medicines, including PD-1/PD-L1 inhibitors, tyrosine kinase inhibitors, and antibody-drug conjugates.

Horizonscan medicines

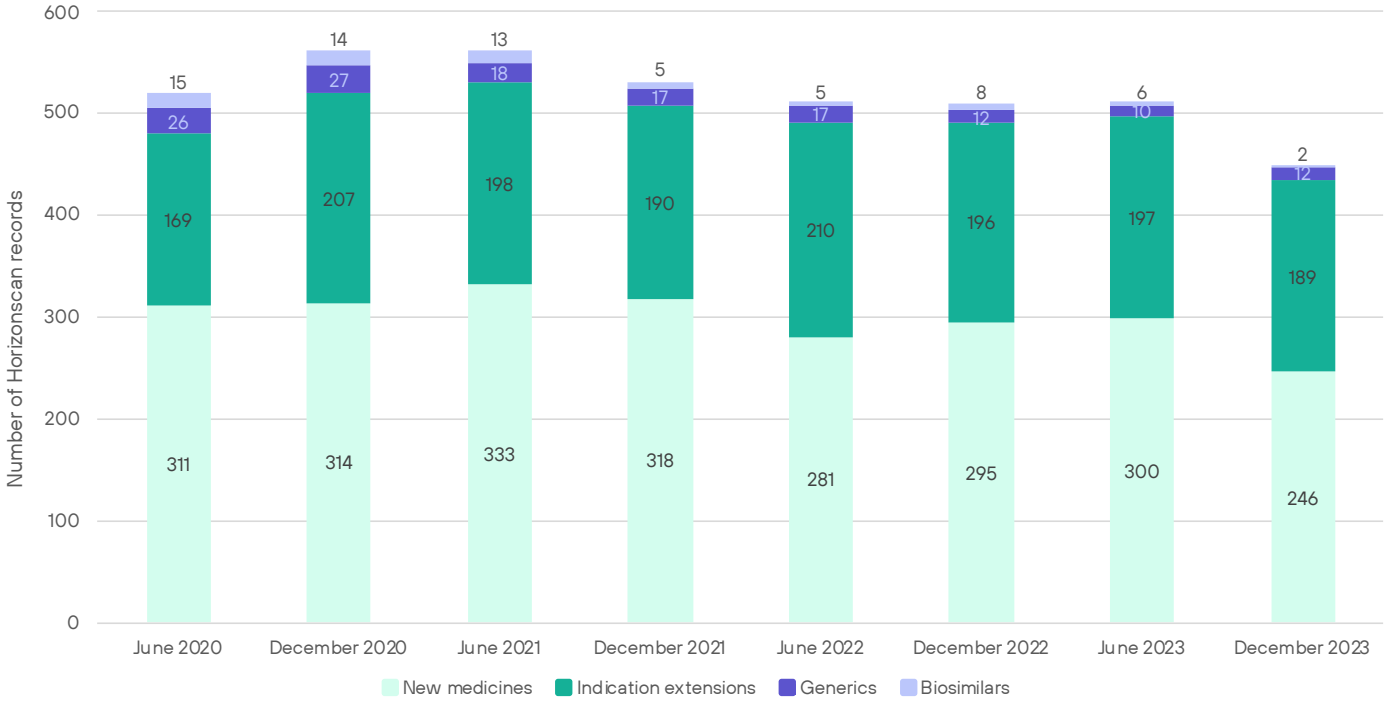
The National Health Care Institute (NHCI) issued the 13th edition of the Horizonscan medicines database on December 5th, 2023[1]. Since 2018, the Horizonscan has been providing an accessible and comprehensive overview of medications projected to become available in the Dutch market within the next two 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 On the Horizon report sheds light on the Horizonscan publications spanning the last three and a half years, encompassing a total of eight releases. The report delves into various aspects, including the number of new medications categorized by disease domain, the expected annual budget impact resulting from the costliest forthcoming medications, and an examination of pharmaceutical interest in specific disease areas. Furthermore, particular focus has been given to the rising trend identified in the anticipated healthcare costs associated with ophthalmological treatments. Possible explanations for this trend are provided in this report’s deep-dive.

The number and type of medicines included in the horizonscan over time

The most recent version of the Horizonscan comprises a total of 449 documented drugs (see Figure 1), indicating a significant decrease in comparison to prior editions. This would signify a reduction in the anticipated number of new drugs entering the Dutch market over the next two years, following a period of stability. In comparison to the reports published in December 2020 and June 2021, there has been a notable decline of around 100 drugs in the expected number of new market entrants. After a quick consultation with the Zorginstituut, we learned that the most significant difference observed in the recent scans lies in the number of medicines that are registered. These resources are usually retained when there is awareness of their association with a reimbursement request. If there are no indications of reimbursement, they are registered and published at most twice. As a result, numerous medicines were excluded during the last scan for this reason. In essence, it is believed that this represents a snapshot rather than a clear indication of a decrease in the influx of innovations.

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



Yet, the authors of this report have identified a trend that could be influencing the decrease in the introduction of new medicines. This trend revolves around the progressively stringent criteria for drug registration and reimbursement in The Netherlands[2]. In recent years, the Dutch Ministry of Health, Welfare, and Sport has heightened its scrutiny on evaluating the cost-effectiveness of new drugs and assessing their broader societal impact. Consequently, a considerable number of experts and opinion leaders have expressed apprehensions about the current and future (speed of) availability of new medicines in the Netherlands, wich is especially concerning for orphan drug companies[3,4].

The most recent compilation predominantly comprises newly introduced medications, constituting 55% of the total, with indication extensions following at 42%, generics at 3%, and biosimilars at 0.5%. Notably, there has been a decline in the representation of biosimilars (from 3% to 0.5%) and generics (from 5% to 3%) from June 2020 to the present within the overall records.

This reduction in the presence of generics and biosimilars raises concerns about potential repercussions on access to affordable treatments and an increase in healthcare expenditures. It underscores the critical need for vigilant monitoring, strategic planning, and prioritization of patient access to essential medications. Ensuring sustainable healthcare systems and the availability of cost-effective options should be a paramount consideration in light of these observed trends. However, it is important to note that only biosimilars that are first to enter the market are included in the Horizonscan.

More and more drugs aimed at skin diseases

Over the past years, the top 10 indications anticipated to have the highest number of new medicines and indication extensions have exhibited a relatively stable pattern, albeit with some notable changes observed in the latest two editions (Figure 2). Lung cancer consistently emerges as an area experiencing continuous growth, ranking first on the list with an expected influx of 32 new medicines and indication extensions in the upcoming years. Last year, we saw a significant surge in the development of medications targeting eye disorders such as age-related macular degeneration (AMD) and diabetic macular edema (DME). However, the expected number of new eye disorders drugs on the market seems to have decreased since last year, while we instead observe a more prominent increase in the number of drugs aimed at skin diseases (4 new drugs added since last edition) and bowel diseases (from 5 drugs included in june 2020 to 10 in december 2023). Remarkably, while the number of new eye disorder drugs has diminished, the total expected costs of these drugs has rapidly increased over the last years, as highlighted in the deep-dive later in this report.

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

Rank	Decmber 2023	Records
	Lung cancer	32
+2	**Skin diseases**	24
-1	Metabolic diseases	19
+1	**Breast cancer**	15
-2	**Eye disorders**	13
+1	**NHL**	12
+1	Bacterial infections	11
-2	**Multiple Myeloma**	10
+2	Bowel diseases	10
	Prostate cancer	10

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 tenth position to the 29th. The current edition includes only four newly developed COVID-19 medicines, in contrast to the fourteen medicines documented in June 2022. As the COVID-19 pandemic has subsided, pharmaceutical industry interest in this domain has markedly declined.

In recent years, there has been an observable trend in certain medical conditions, with some showing an increase in the inclusion of new drugs in the Horizonscan, while others have experienced a decline (Figure 3). Even in areas with significant unmet needs, such as bacterial infections, diabetes, or the facilitation of stem cell transplantations, the number of new medicines has notably decreased. This decline is concerning, especially in the context of pressing global health challenges, such as antimicrobial resistance (AMR). Antimicrobial resistance is a substantial threat to public health worldwide, directly causing 1.27 million global deaths in 2019 and contributing to 4.95 million deaths[5]. The World Health Organization (WHO) already warned that there is an inadequate research and development pipeline in the face of rising levels of AMR, and that there is an urgent need for additional measures to ensure equitable access to new and existing vaccines, diagnostics, and medicines.

Fig 3: **Top rising and falling indications by change in number of Horizonscan records**

Inclusion filter: New medicines & indication extensions

Timeline: December 2023 publication compared with June 2020 publication

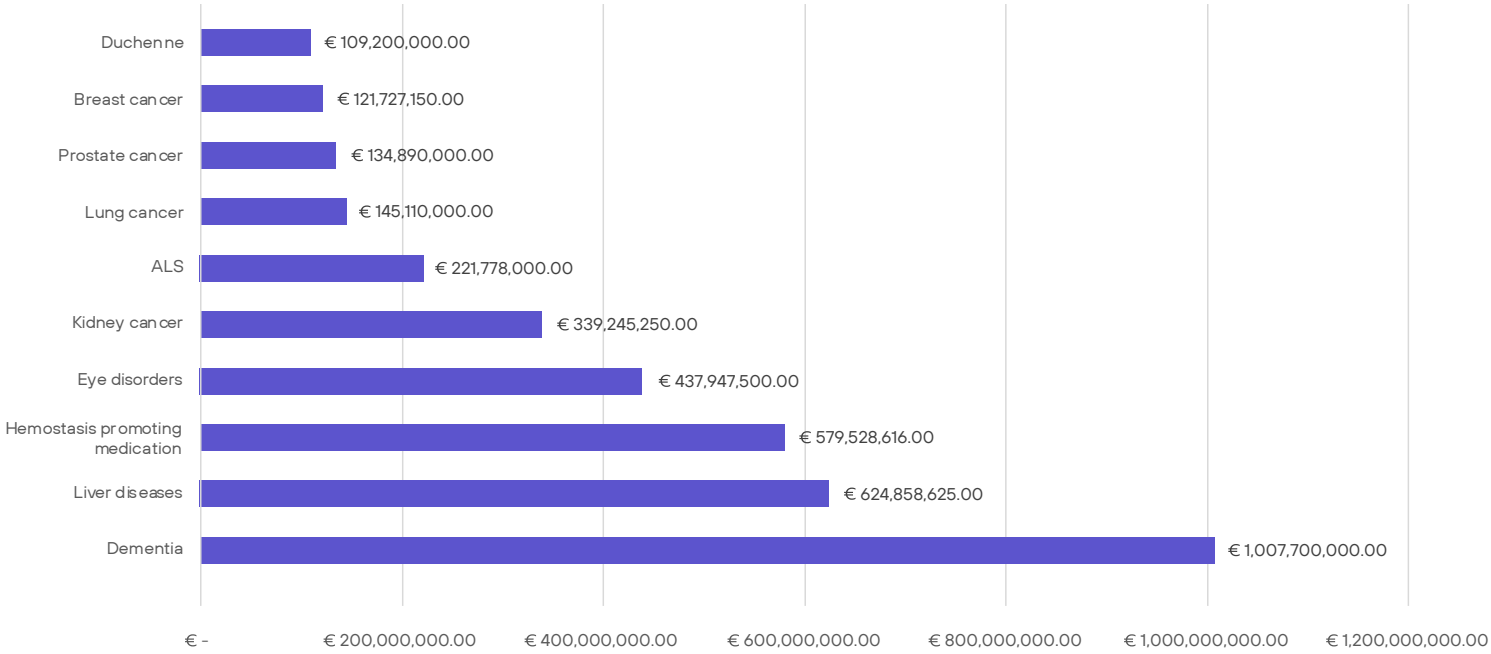
The annual budget-impact of new medicines

In Figure 4 below, the top ten indications are outlined, revealing the anticipated highest annual budget impact on the Dutch healthcare system. It should be noted that the costs presented here only give an indication on the real total costs, as it is the result of the average expected patient volume times the average cost per patient, both per year. Notably, there is a significant financial burden expected for liver diseases, primarily propelled by the developments in nonalcoholic fatty liver disease (NAFLD or NASH in Dutch) treatments. The rising expected budget impact of Dementia is noteworthy and can be attributed to two drugs, lecanemab and donanemab, manufactured by Eisai and Eli Lilly, respectively. These drugs have garnered global attention for their potential in treating early Alzheimer's disease, with donanemab recently demonstrating a 35% reduction in cognitive decline in clinical trials[6]. However, caution is advised by experts, as the full results are yet to be published. Questions linger regarding the clinical usefulness of the drugs and whether the modest benefits outweigh potential harmful side effects. This underscores the importance of thorough scrutiny and a comprehensive understanding of the risks and benefits before determining the clinical utility of these medications.

Fig 4: **Expected annual budget impact of the most expensive indications**

Inclusion filter: New medicines & indication extensions

Timeline: December 2023 publication



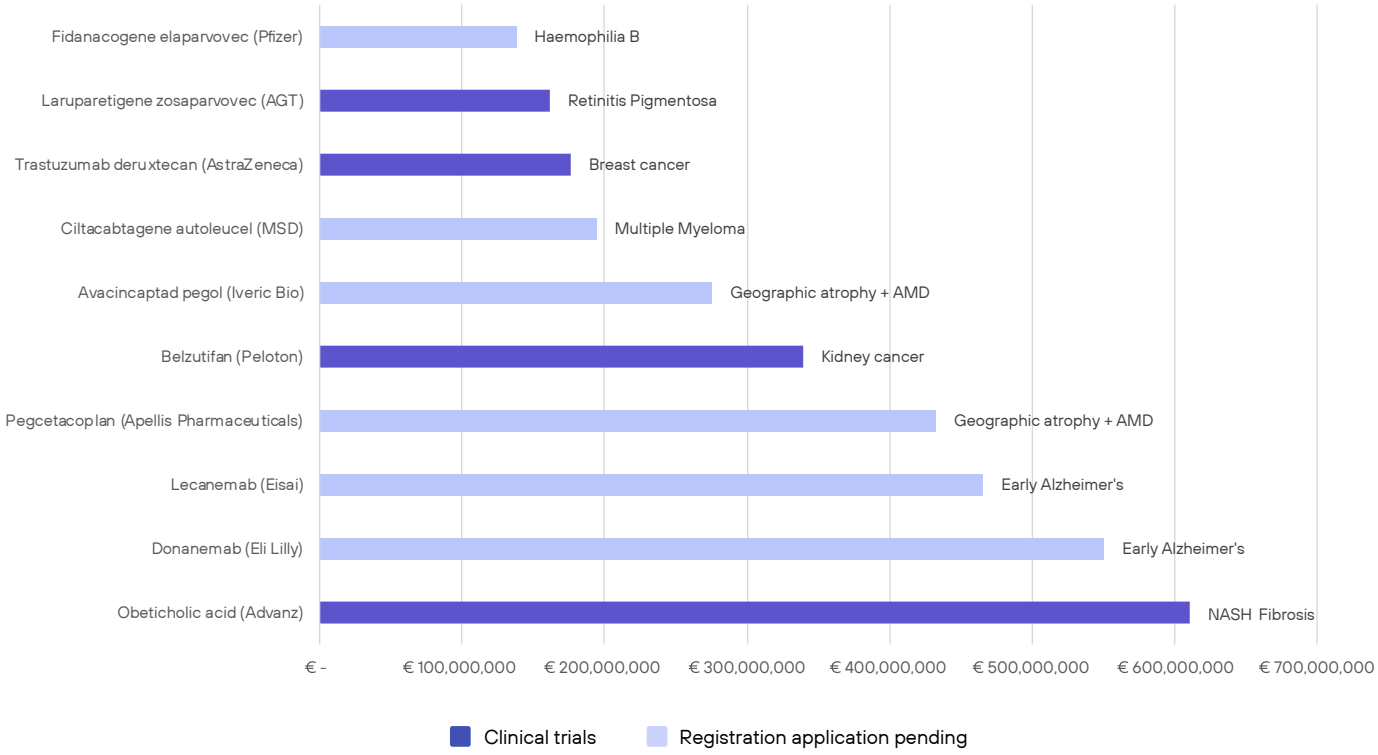
Once again, it's crucial to note that the total costs presented in this analysis are merely estimates. For instance, the current price in the Netherlands is uncertain and is currently based on the annual costs per patient in the US. Additionally, the number of patients treated with these medicines will depend on factors like their relative effectiveness and the market share each medicine attains over time. Therefore, a more realistic expectation is that only one of the medicines will meet the projected total costs, while the other may only contribute a fraction, effectively halving the overall anticipated costs of these medicines. Nonetheless, despite this potential variation, the projected budget impact is still considered significant.

Provided below is a summary of the anticipated overall expenses associated with the ten most costly drugs projected to enter the market within the next two years, providing a glimpse into the magnitude of forthcoming medications (Figure 5). Unsurprisingly, the top three positions are occupied by the two Alzheimer's drugs from Eisai and Lilly, along with a treatment for NAFLD.

Fig 5: **Expected annual budget impact of the most expensive drugs with registrations in the coming 2 years**

Inclusion filter: Top 10 expected most expensive new medicines & indication extensions

Timeline: Expected registration from December 2022 to December 2024



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)[7] underscores the necessity of making prudent decisions regarding the allocation of our collective financial resources.

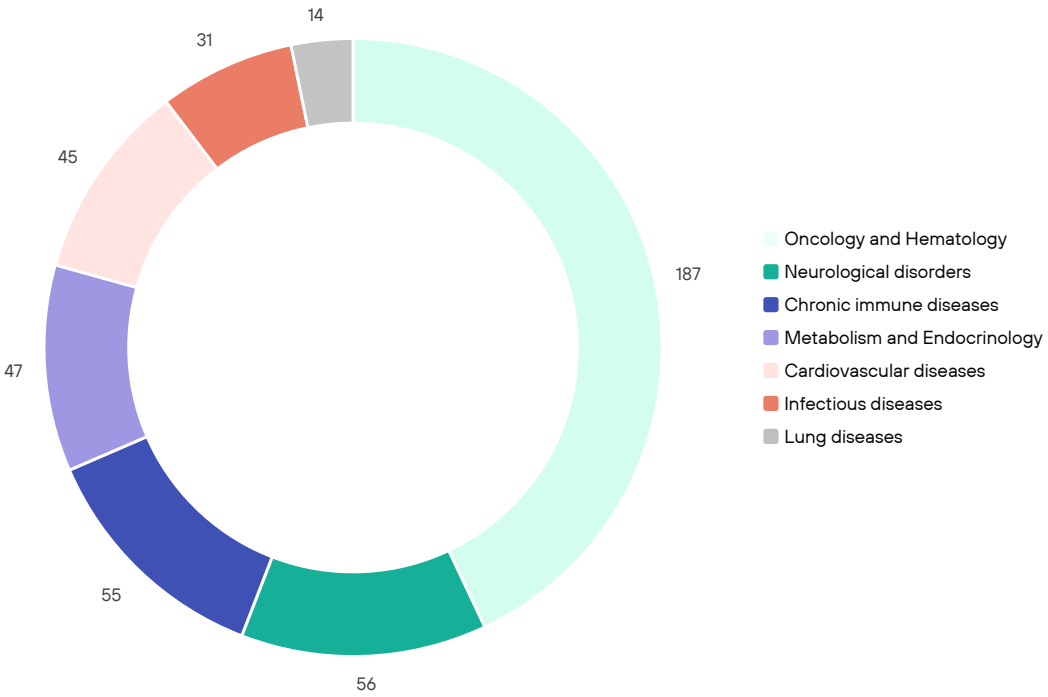
Many new medicines in the oncology & neurology pipelines

In terms of overall distribution, the majority of medications included in the Horizonscan database target oncological, hematological, and neurological diseases (Figure 6). These domains encompass conditions like lung cancer, breast cancer, multiple myeloma, as well as neurological disorders affecting the eyes and muscles, such as AMD, DME, Duchenne, and generalized myasthenia. This trend has demonstrated relative stability over the years, with limited fluctuations in the composition of these therapeutic domains.

Fig 6: **Horizonscan records by disease domain**

Inclusion filter: New medicines & indication extensions

Publications filter: December 2023 publication

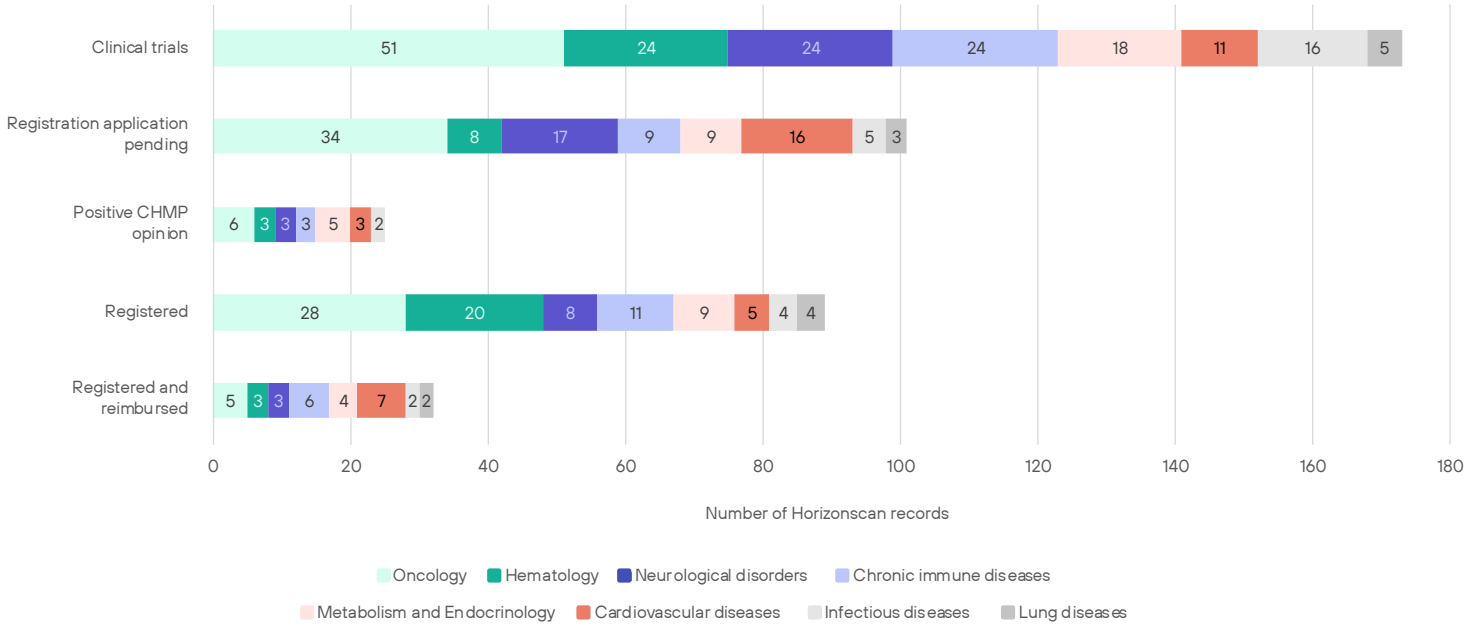


Upon further analysis of the medicines' distribution based on their lifecycle phases, it becomes apparent that a substantial portion of the medications featured in the Horizonscan is currently still in the clinical trial phase. Within this subset, again, a significant emphasis is placed on oncological and hematological diseases (Figure 7).

Fig 7: **Horizonscan records by disease domain per lifecycle phase**

Inclusion filter: New medicines & indication extensions

Publications filter: December 2023 publication



Deep dive: Ophthalmology

Ophthalmological drugs, vital for preserving and enhancing vision, have been pivotal in addressing various eye conditions and diseases, such as AMD, DME, and retinal vein occlusions (RVO). Newly developed ophthalmological drugs are increasingly focusing on extending the interval of intravitreal injections while maintaining or improving outcomes, a critical aspect in enhancing patient experience and treatment efficacy. This deep dive delves into the overall trends surrounding the development and costs of ophthalmological drugs in the Dutch market.

Fig 8: **Number of ophthalmological drugs in Horizonscans over time**

Inclusion filter: New medicines & indication extensions
Timeline: June 2020 publication - December 2023 publication

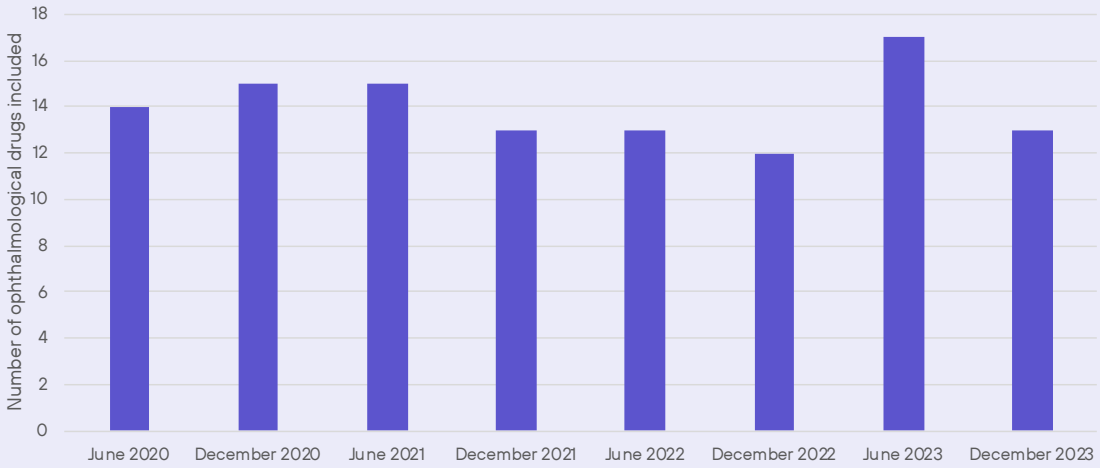


Figure 8 reveals a stable trend in the development of new ophthalmological drugs in the Dutch market. This stability, spanning several years, implies a sustained commitment to research and development within the pharmaceutical sector, emphasizing the ongoing importance of addressing ocular health. It also suggests a steady influx of innovative drug candidates and an enduring interest in advancing treatments for diverse eye disorders. The constancy in new drug approvals may be attributed to continuous investments in ophthalmic research, coupled with advancements in understanding the intricate nature of ocular diseases.

Fig 9: **Total expected costs of ophthalmological drugs in Horizonscans**

Inclusion filter: New medicines & indication extensions

Timeline: June 2020 publication - December 2023 publication

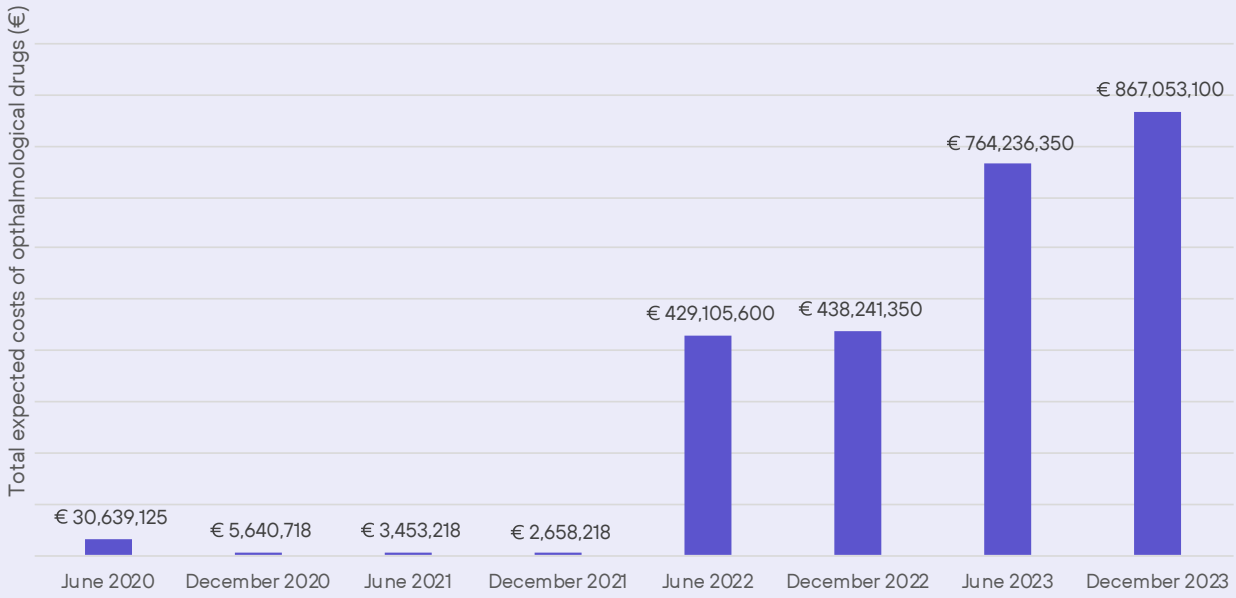
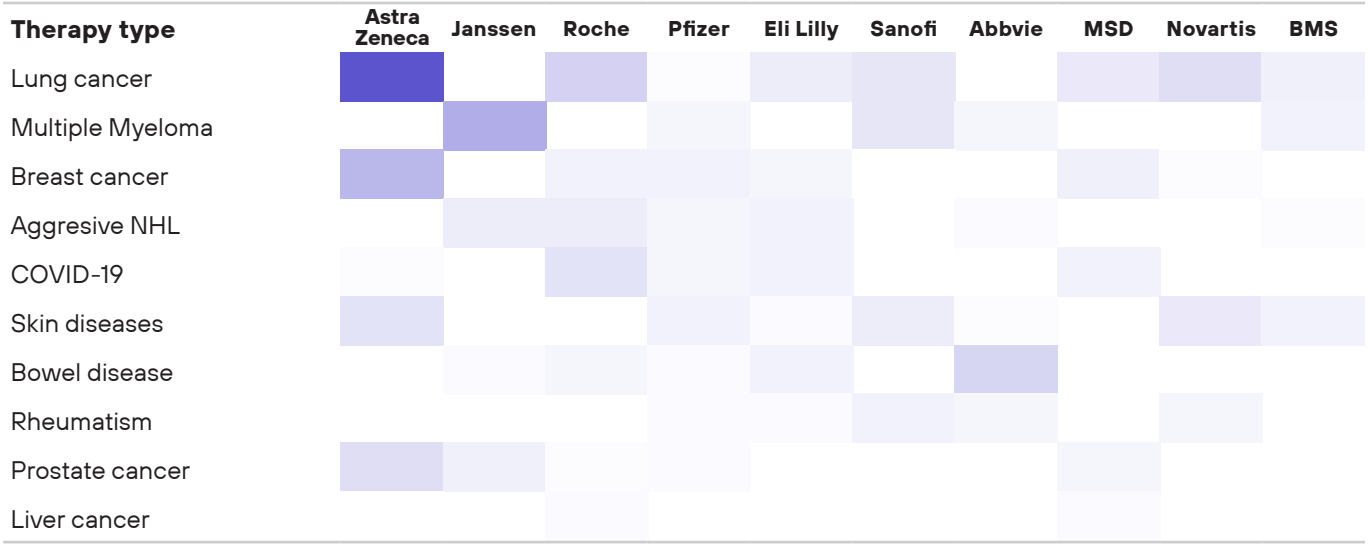


Figure 9 highlights a marked increase in the expected total costs linked to ophthalmological drugs over the years. This surge in costs can be attributed to several factors, notably the complexity of developing specialized and targeted eye drugs, alongside anti-VEGF agents like ranibizumab, aflibercept, and brolucizumab[8,9]. Biologics, while offering targeted and personalized treatments, often come with a higher production cost compared to traditional pharmaceuticals. This contributes significantly to the observed escalation in overall expenses. The demand for more effective therapies with larger injection intervals, combined with increased industry standards for safety and efficacy, leads to prolonged research and development timelines, further amplifying costs.

Mapping the interest of pharma in different disease areas

To offer a comprehensive overview of the top 10 indications featuring the highest influx of new medications and indication extensions from pharmaceutical companies over the past three years, we present a heatmap in Figure 10. The heatmap reveals a prominent presence of AstraZeneca and Roche in oncological indications, particularly lung and breast cancer. This is evident from the substantial introduction of new medications in these areas consistently across each Horizonscan publication. Notably, Janssen stands out for its emphasis on multiple myeloma, although it is intriguing that recent Horizonscan editions do not mention any breast cancer medications from Janssen.

Fig. 10: **Overview of the most frequently included therapy types in the Horizonscan per manufacturer**



An intriguing observation is that bacterial infections, eye disorders, diabetes, and metabolic diseases are typically covered by only three or four of the top 10 pharmaceutical companies. This phenomenon can be explained by the varying strategic focuses and therapeutic areas of interest for pharmaceutical companies. Bacterial infections may be receiving less attention due to challenges in developing new antibiotics and the associated regulatory hurdles. Eye disorders, diabetes, and metabolic diseases might be areas where companies perceive a saturation of available treatments or face high competition, leading to a more concentrated effort by a select few in these domains. This observation underscores the nuanced and strategic nature of pharmaceutical companies' priorities in addressing medical conditions.

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[10]. 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[11].
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.

Also, through our recent collaboration agreement[12] 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 an examination of the rising costs of ophthalmological drugs. 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.

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.

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