EXECUTIVE SUMMARY

Anual Report on ACCESS 2024

to Orphan Medicinal Products in Spain

aelmhu

Access to orphan medicinal products (OMPs) with orphan designation and trade name as of 31 December 2024.

INDEX

01 ACCESS REPORT AELMHU

The Spanish Association of Orphan and Ultra Orphan Drug Laboratories (AELMHU) presents, once again, the main **conclusions of its Annual Report on Access to Orphan Medicinal Products (OMPs) in Spain.**

This document analyses the situation of products with a trade name and orphan designation by the European Medicines Agency (EMA) as of 31 December 2024, as well as the procedure they have followed to reach the Spanish market, from the assignment of the National Code (NC) by the Spanish Agency of Medicines and Health Products (AEMPS) to public reimbursement.

For more than 14 years, AELMHU has been working to offer more and better indicators that allow all those interested stakeholders - patients, the scientific community, health care professionals, industry, public decision-makers and society in general - **to have** regularly **updated data** on access to, and availability of innovation in a field as complex and, at the same time, as promising, as **treatments for rare diseases.**

It is a real responsibility for our Association to know that our reports have become the **main reference** for data on access to orphan and ultra-orphan medicines in Spain. To continue improving the information available, we are working and extending last year's line of work, in areas such as those orphan treatments that have Marketing Authorisation but do not yet have a National Code in our country, timelines and their therapeutic areas. Also, **we have updated our proposals to improve the situation of orphan medicines in Spain to collaborate in the dialogue and consensus with all the agents involved**. This collaboration and dialogue will be even more important given the regulatory developments expected for 2025 and subsequent years.

In the political context, 2024 has been a year marked by different initiatives towards transforming the National Health System (NHS), with the aim of laying the foundations for a regulatory package that is expected to be published and approved during 2025 and 2026. In this regard, two Bills, the National Health System Universality Bill and the Equity and Cohesion Bill, are still in the amendment phase for debate in the Congress' Health Commission, similarly to the Bill on the National Public Health Agency. Other regulatory developments that have materialised this year include the Draft **Royal Decree regulating the procedures for the reimbursement and pricing of medicines**, currently in the public consultation phase, and the **Royal Decree regulating the evaluation of health technologies**, the text of which is awaiting publication. However, we are waiting for the reform of the Law on Guarantees and Rational Use of Medicines, now called the **Law on Medicines and Medical Devices**.

Importantly, at the end of 2024, the **Pharmaceutical Industry Strategy** was published, whose objective is to set the roadmap for the sector over the next four years and of which **AELMHU is a member**.

We are facing a great opportunity to move towards a more inclusive, innovative and sustainable model that takes into account the needs of patients with rare diseases. In this regard, the Strategy has recognised the significant burden that **rare diseases** pose for patients and families, marking it as a **strategic and priority therapeutic area of work**, similarly to advanced therapies given that in most cases they are treatments for rare diseases.

Likewise, the Ministry of Health presented the **"Evaluation of the Rare Diseases Strategy of the National Health System 2024"** Report, which is expected to provide a boost to the renewal of the Rare Diseases Strategy, approved in 2009 and updated in 2014.

At the European level, the European Parliament has approved, by majority, the implementation of the **European Pharmaceutical Strategy, the European Regulation on Health Technology Assessment (HTA)** has been activated since January 2025, and the Spanish Agency for Medicines and Health Products (AEMPS) is working on its implementation at the national level.

AELMHU has participated in all relevant consultations related to orphan medicines and rare diseases at regional, national and international levels, and the Access Report is an example of how **the association wants to continue projecting more and better indicators to contribute to the common goal of speeding up the availability of pharmaceutical innovation in Spain.**

AELMHU is a non-profit organisation that brings together pharmaceutical and biotechnology companies **with a strong commitment to research, develop and commercialise innovative therapies to improve the quality of life of patients suffering from rare and ultra-rare diseases.**

The organisation's mission is to contribute to improving the **health and quality of life of people affected by rare diseases**, giving visibility to the pathologies and highlighting the value of the research and treatments available for them.

AELMHU's current **members** are: Alexion AstraZeneca Rare Diseases, Alnylam Pharmaceuticals, AOP Health, Argenx, Ascendis Pharma, Biocryst, Biogen, BioMarin, Chiesi, Csl Behring, Italfarmaco Group, Horizon, Immunocore, Insmed, Ipsen, Jazz Pharmaceuticals, Kyowa Kirin, Novartis, PTC Therapeutics, Sanofi, Sobi, Takeda, UCB, Ultragenyx Pharmaceutical and Vertex.

02 METHODOLOGY

The methodology for the 2024 Annual Report on Access to Orphan Medicines in Spain consists of four phases:

01 Identification of medicines with a valid orphan designation and trade name as of 31 December 2024

An orphan designation (OD) is granted during the early stages of a medicine's research programme. Of the more than 2,9000 active ingredients that have received this OD from the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA), those with an active ingredient as of 31 December 2024 (more than 2,000) have been identified. Of these, those with a trade name are identified (more than 250), excluding their new presentations or indications.

Overall, **210 orphan medicines with a commercial name and with an active orphan designation** as of 31 December 2024 are identified.

02 Orphan medicines with marketing authorisation but excluded from the European Register

We then identified which of these orphan medicinal products have been withdrawn (or have not yet been included) in the European Commission's Community Register of Orphan Medicinal Products for marketing in the EU (n=63). As a result, the number of **orphan medicines with a marketing authorisation** (MA) as of 31 December 2024, in EU countries is obtained (**n=147**).

03 Orphan medicines with a National Code

The third step was to identify which of those 147 orphan medicines have been granted a **National Code (NC)** by the AEMPS in Spain (**n=131**).

04 Orphan medicines reimbursed by the NHS

Finally, the **orphan medicines which are reimbursed by the NHS**, according to the information contained in the Nomenclator of the Ministry of Health, are identified (**n=85**). The date of the first positive reimbursement decision for each orphan medicine is reported.

03 CURRENT CONTEXT OF ORPHAN MEDICINES

Orphan medicines are intended to establish a diagnosis, prevent or treat patients suffering from a **rare or minority disease** with no therapeutic alternative. They are **innovative medicines**, most of them of biotechnological origin.

Rare diseases form a very heterogeneous group of diseases whose main common characteristic is their **low prevalence**, about **80% are of genetic origin and a high percentage manifest themselves in paediatric age.**

Currently, rare or minority diseases **affect less than 5 out of every 10,000 people who have no alternative treatment**. These are **serious, chronic and disabling** diseases that in a high percentage of cases compromise the lives of patients.

It is estimated that there **are** more than **6,300 rare diseases** in the world**, of which only 6% have some kind of diagnostic tool or treatment**, making research and innovation in this field an urgent need for society as a whole.

Aware of this situation, the European Parliament and the EU Council approved **EU Regulation 141/2000, which is still awaiting an update**, and which established that "patients affected by rare diseases should be entitled to the same quality of treatment as other patients", incorporating incentives to improve knowledge and research, development and marketing of medicines in the field of rare diseases.

Since then, **the legislation promoted by the EU and Spain has made unquestionable progress**. In fact, especially in recent years, **the research efforts of pharmaceutical companies** have been strengthened and the willingness of a growing number of companies capable of providing innovations in this field has increased.

This effort continues to be a priority, reflected in the latest **Annual Report on Clinical Trials in Rare Diseases in Spain in 2023**, prepared by AELMHU. On a positive note, we observe the increase in the number of clinical trials in the early stages of development; however, there is a 10% decrease in the total number of authorised clinical trials from previous year (233 vs.190).

According to AELMHU analysis, based on the Spanish Registry of Clinical Trials (REec), which depends on the Spanish Agency of Medicines and Health Products (AEMPS), **the pharmaceutical industry continues to be the main driver of clinical trials in rare diseases in Spain,** representing 96%, one point more than in 2022, showing a clear commitment to research in this area.

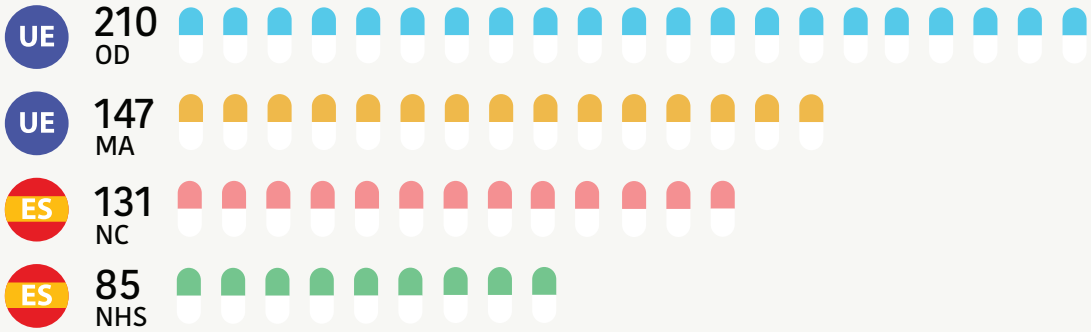
However, there are several **areas for improvement** so that the industry's interest in delving deeper into such a complex field as rare diseases is directly reflected in a better and faster availability of orphan medicines for patients.

In this sense, AELMHU wants to continue analysing in depth numerous aspects such as **equity in access** to these treatments or the **streamlining of** bureaucratic **processes** to facilitate **effective access** to a unique opportunity for many people suffering from this type of pathologies and who have not found a therapeutic alternative.

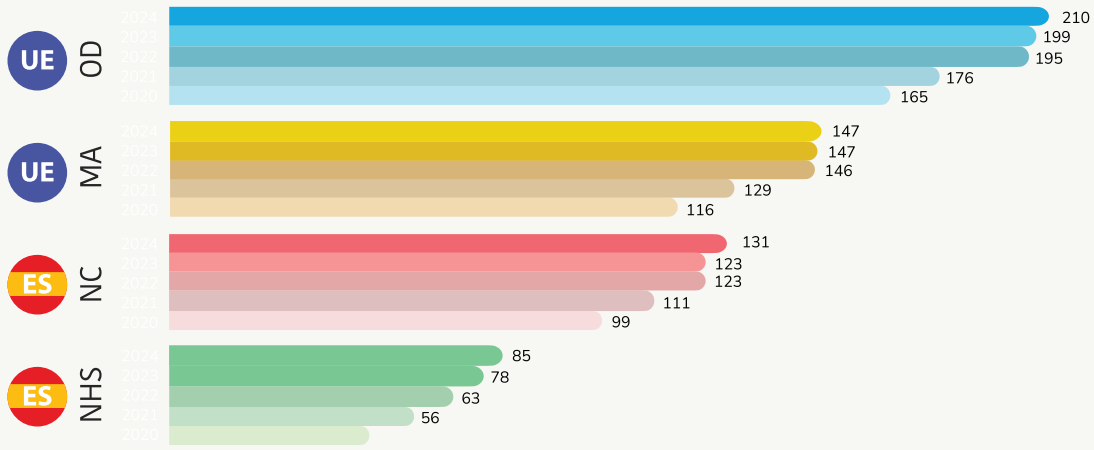
04 ORPHAN MEDICINES IN THE EU AND SPAIN IN 2024

Year 2024 closed with **210 orphan medicines with a valid orphan designation** and trade name in the EU, of which **147 have an EU marketing authorisation, 131 received a National Code** in Spain (89%) and **85 are reimbursed** by the National Health System (58%).

Key indicators in the EU and Spain



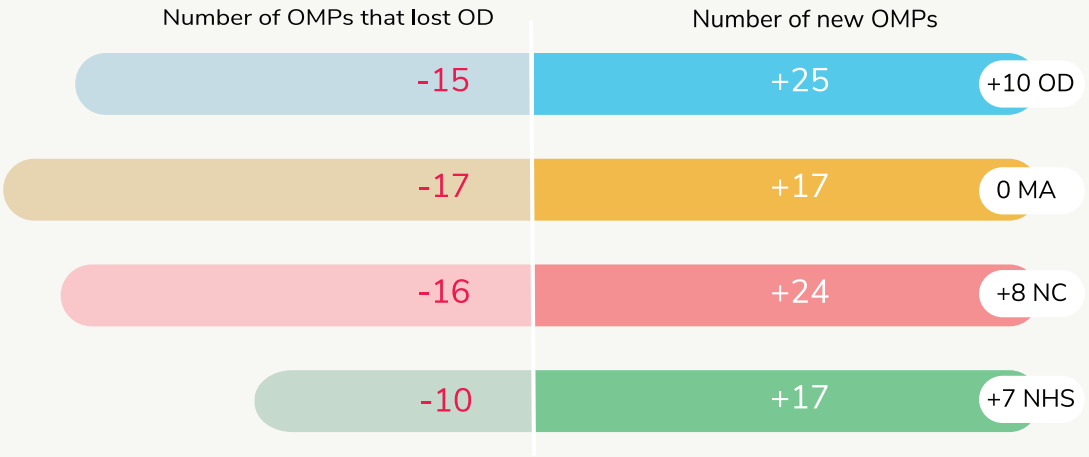
Evolution of the indicators in the EU and Spain 2020-2024



During 2024, all **the indicators reported here for orphan medicines in the EU and in Spain improve**, although it is important to note that with **different magnitude.** The greatest increase is observed in orphan designations, followed by treatments that obtain National Code and then those that are reimbursed.

These indicators also take into account, as detailed below, treatments that have lost their orphan designation and/or marketing authorisation in 2024 and are therefore excluded from the relevant sample for the study.

Variation in the indicators 2023 - 2024



This Figure details the number of **orphan medicine that have lost orphan designation** during 2024 and would therefore be excluded from the analysis: 15 medicines with trade name without MA, 17 with MA, 16 with NC and 10 reimbursed. Thus, the main results in **net terms for 2024** are as follows:

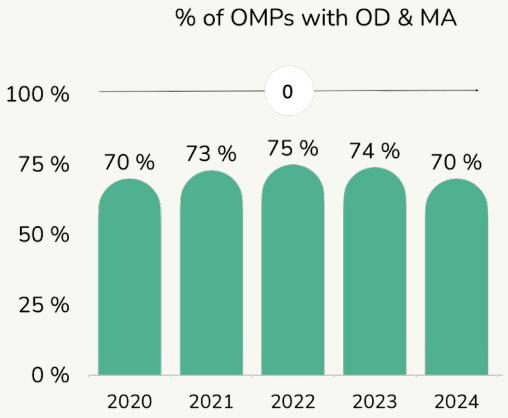
- Increase of 11 new positive designations[2].
- Increase of 1 MA.
- Increase of 8 NCs.
- Increase of 7 new orphan medicines reimbursed.

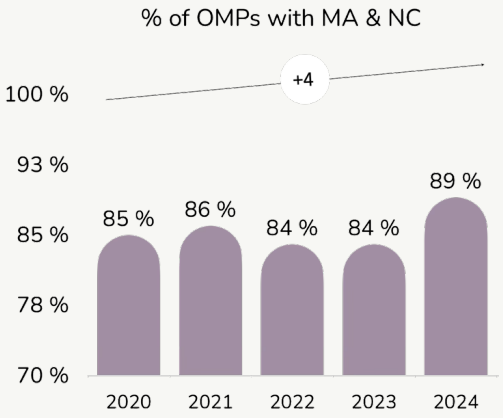
[2] Due to a failure to update the EMA website between December 2023 and April 2024, the medicine TAVNEOS was not included in the 2023 MMH annual report. This error was corrected in the report for the first four months of 2024. However, in the 2023 vs. 2024 annual comparison, the total number of medicines with ODs has an adjustment for this reason (199 ODs from 2023 + 25 added - 15 eliminated + TAVNEOS = 210 OD).

Comparison across indicators

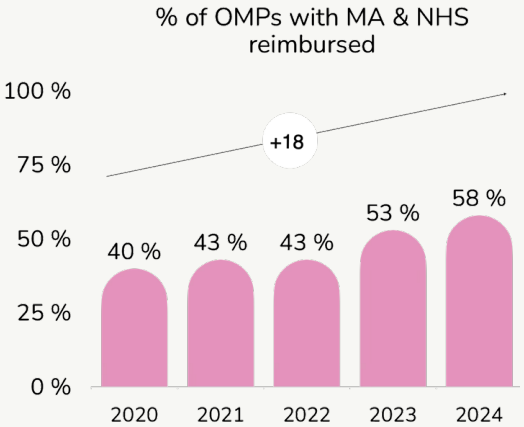
As the following graphs show, **70% of all orphan-designated medicinal products with a valid orphan designation and trade name have an EU marketing authorisation**, which represents a reduction of 4 percentage points compared to the figure for 2023 and equals the minimum since 2020.

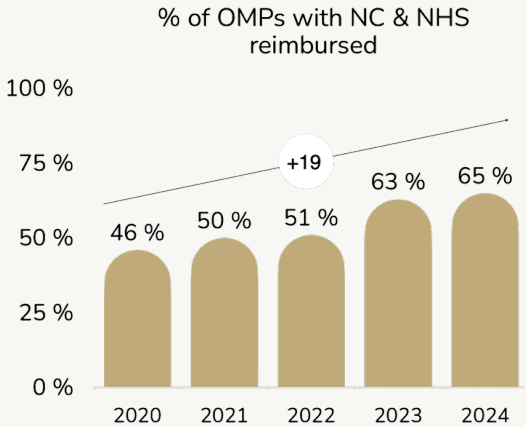
On the other hand, the proportion of **National Code** applications **in Spain** for those **orphan medicines with a MA in 2024 increases to 89%**, the highest percentage during the last five years .





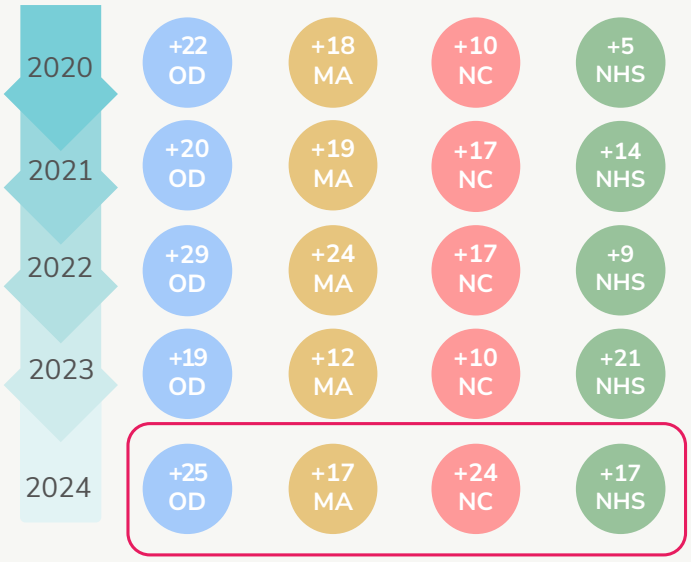
Orphan medicines reimbursed by the NHS in 2024 represent **58% of those with MA and 65% with NC**; the increases are 5 and 2 percentage points respectively from 2023. Below we delve into the orphan medicines reimbursed in 2024.





Status of new orphan medicines by year and by indicator

The following graph shows the evolution of the main indicators: new designations, marketing authorisations, national codes and new products reimbursed in Spain, year by year since 2020.

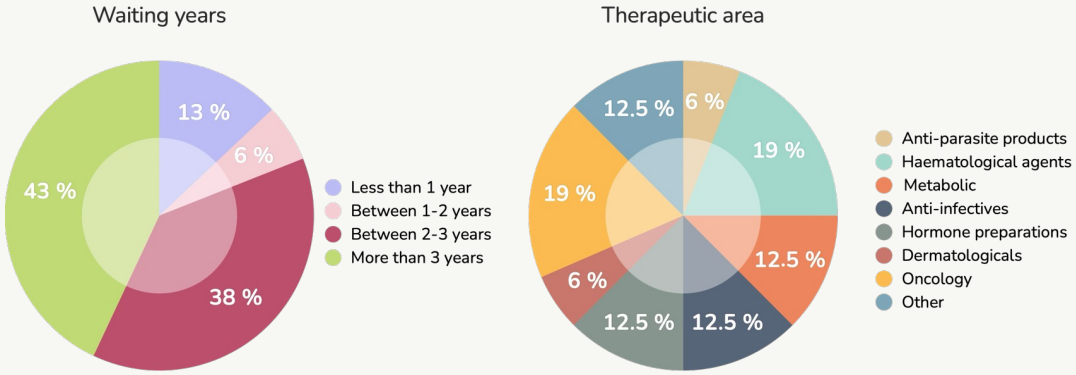


In absolute terms, the evolution of all indicators improves in 2024. If we compare them with the previous year, we see considerable increases in the first 3 indicators (OD, MA and NC). **The 140% increase in National Codes** deserves special mention. However, the number of reimbursed OMPs is lower than in 2023, a particularly good year for this indicator.

05 ORPHAN MEDICINES WITH MARKETING AUTHORISATION WITHOUT NATIONAL CODE IN SPAIN IN 2024

As of 31 December 2024**, there were 16 OMPs with marketing authorisation that had not yet arrived in Spain** (without NC), which represents 11% of those authorised at the community level. There is a significant reduction in this percentage in 2024, making this proportion the lowest in the last five years.

If we look at the time elapsed since these treatments obtained marketing authorisation, we can see that 13% obtained it less than 1 year ago, 6% between 1 and 2 years ago, and the remaining 81% more than 2 years ago. This last percentage is the one that has grown the most with respect to 2023, when the percentage of medicines that had obtained marketing authorisation more than 2 years ago was 37 %.

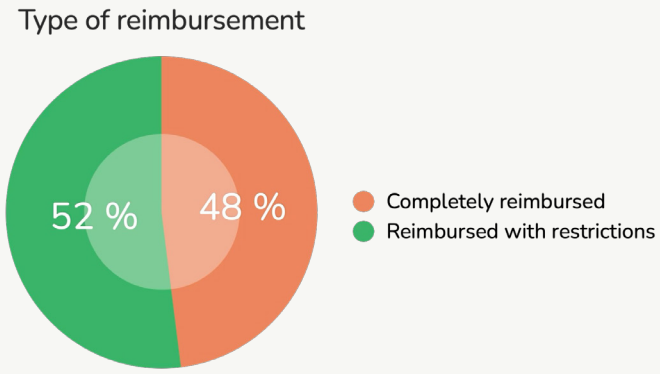


By therapeutic area, haematological and oncological agents become the predominant areas (19% each), followed by anti-infectives, metabolic and hormonal preparations (12.5% each respectively).

06 ORPHAN MEDICINES REIMBURSED IN SPAIN

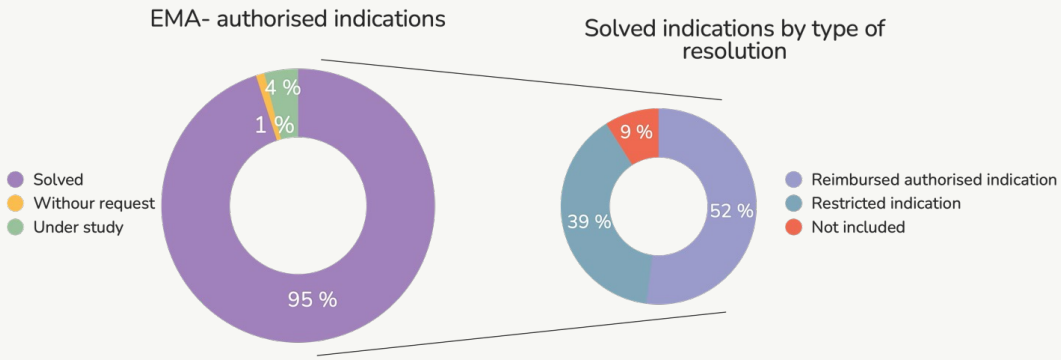
Medicines reimbursed in Spain

As of 31 December 2024, **85 orphan medicines** are **reimbursed in Spain**, which represents 65% of the total of the 131 orphan medicines with a National Code. This percentage is **2 points higher than in 2023** .



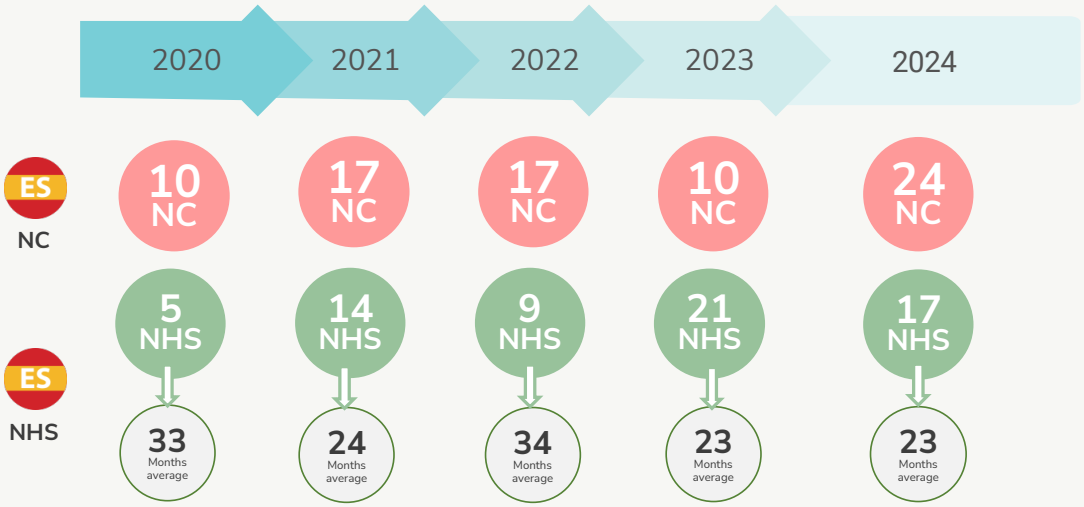
Of these 85 medicines with a positive pricing and reimbursement resolution in the NHS, and as the above graph indicates, **52% (44) are reimbursed with restrictions**, either due to restrictions in the authorised indication(s), or because they have an indication not reimbursed.

In addition, these 85 medicines have a total of 115 indications authorised by the EMA and, of these, 59 are reimbursed without any restrictions, as detailed in the following figure :



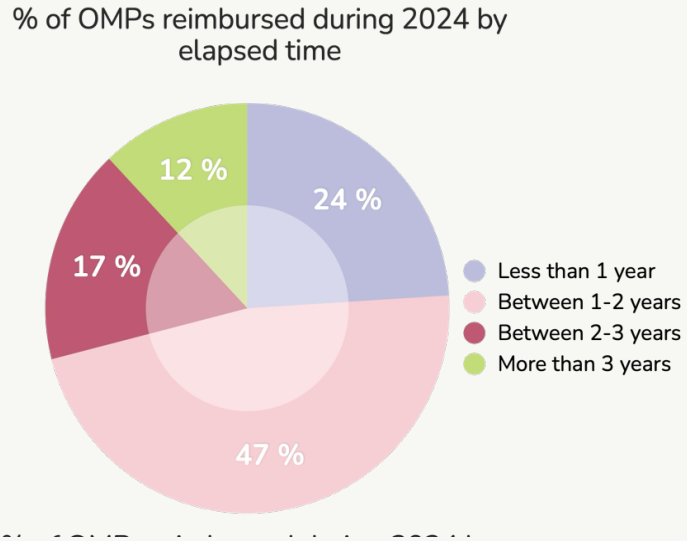
Medicines reimbursed in 2024

En el ejercicio 2024 se financiaron en España **17 nuevos medicamentos huérfanos:** 9 durante el primer cuatrimestre, 3 en el segundo cuatrimestre y 5 en el tercero. La cifra del 2024 es la segunda más alta de los últimos 5 años, solo por debajo del máximo histórico de 2023.



For these 17 medicines, the average time elapsed between the EU marketing authorisation and obtaining the National Code was 6 months, while **the time from the NC to their incorporation into the NHS was 23 months**, both the same as in 2023. It is important to continue working on reducing these timelines.

Moreover, almost half of the 17 medicines have waited an average of between 1 and 2 years to obtain reimbursement, and 30% more than 2 years.

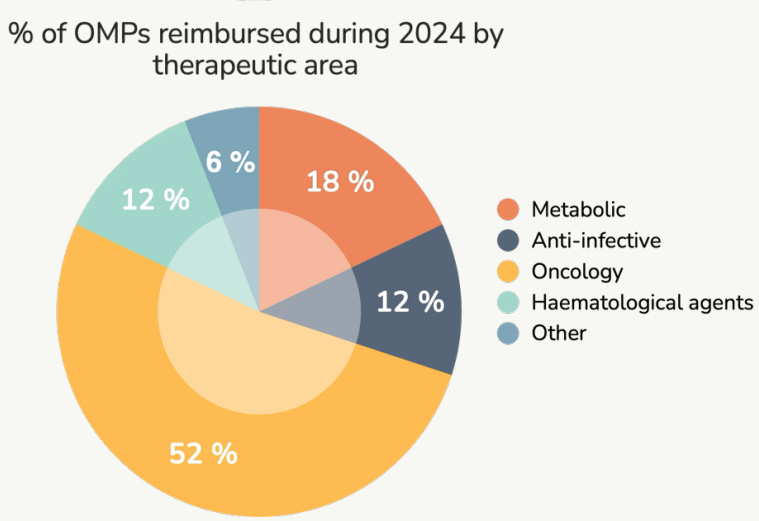


On the other hand, **41% of the 17 new products reimbursed during 2024 have restricted funding** (based on EMA-approved indications) and **100% of them have conditional funding.**

In addition, 15 of the 17 medicines have monitoring conditions and **16 are subject to two or more reimbursement conditions.**

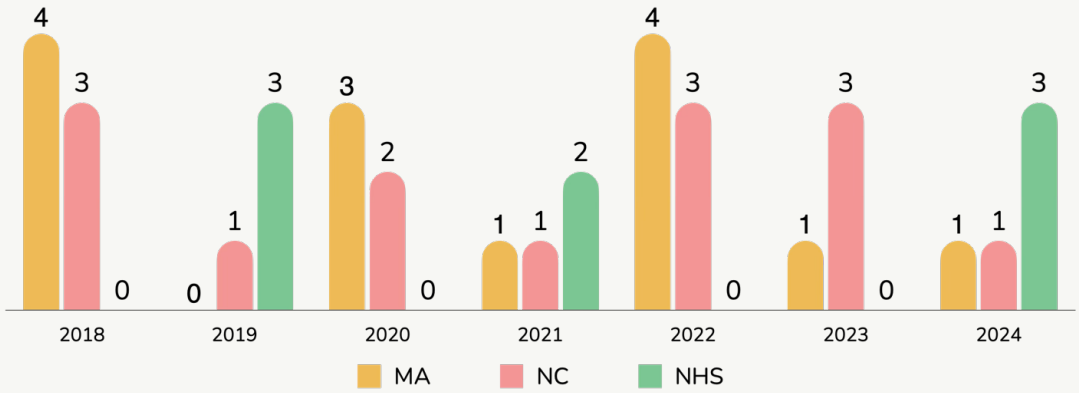
We also note that 16 of the 17 OMPs have been considered at least twice by the Interministerial Medicines Pricing Commission (CIPM), and of these, 8 were considered 3 times. In fact, all the treatments were reimbursed according to criteria (a) and (c) included in the current legislation, which refer to the severity, duration and sequelae of the pathology, and the therapeutic and social value of the medicine, respectively.

Finally, more than 50% (9) are for oncological diseases and 18% (3) for metabolic diseases .



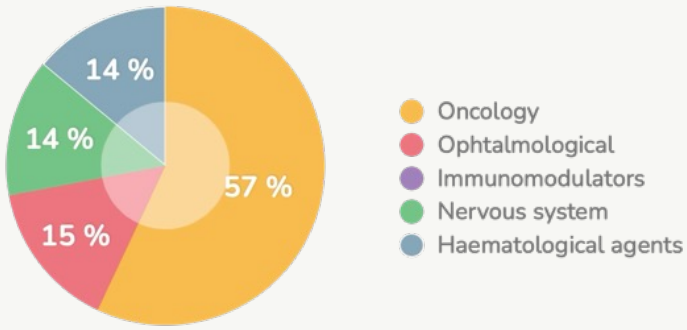
07 ADVANCED THERAPY MEDICINAL PRODUCTS (ATMPS) WITH ORPHAN DESIGNATION

As of 31 December 2024, there are 15 advanced therapy medicinal products with orphan designation and marketing authorisation. Of these, 14 have a National Code, although only half are financed by the NHS (7). Of the remaining 7 therapies with NC, but not reimbursed, 5 have an unfavourable resolution, and 2 are under evaluation or without a request for reimbursement.



It is important to highlight that in 2024 Spain incorporated 3 ATMPs with orphan designation into the NHS; this is a milestone considering that the last one was reimbursed in our country in 2021.

Four of these therapies are oncological and the rest are: 1 ophthalmological, 1 immunomodulatory and 1 for the nervous system, respectively. In addition, all 7 therapies are included in Seguimed. and Valtermed, and six have at least two additional financing conditions, including payment by results (6) and price review (3).

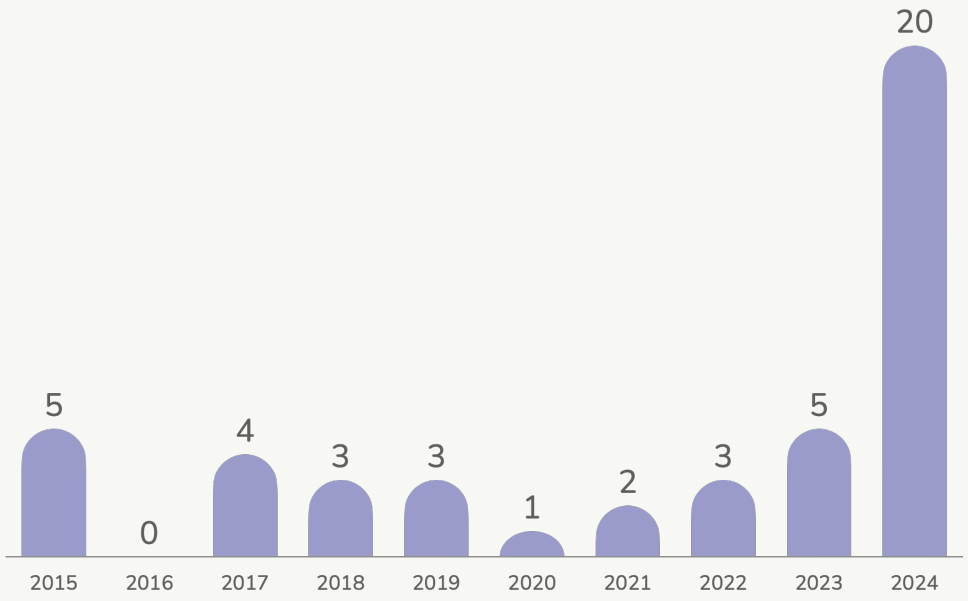


Finally, **33 advanced therapies with OD** are included in the EMA's **PRIME program**, which is intended to support the development of medicines targeting unmet medical needs, and another **5 are under evaluation by the CHMP**.

On the other hand, this Executive Summary includes, as a novelty, information on academic advanced therapies, since authorisation for use has been given to 2 of these therapies in 2024; in total, and as of 31 December 2024, 5 of these academic therapies have been granted an authorisation for use.

08 ORPHAN MEDICINES NOT REIMBURSED

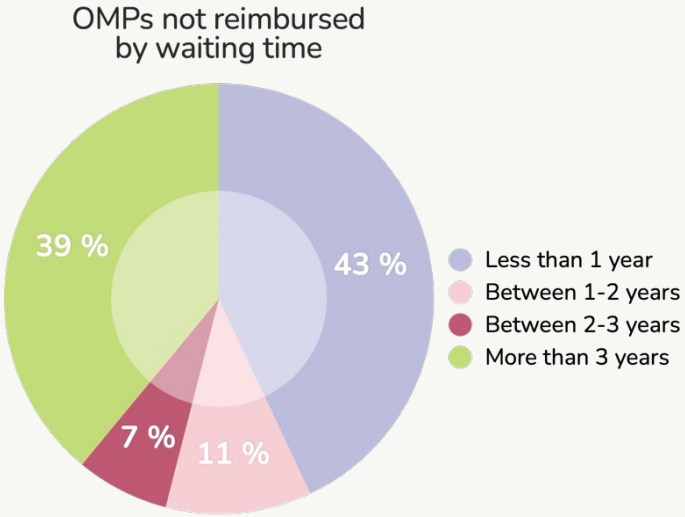
There are currently **46 orphan medicines not reimbursed** in Spain, one more than in 2023. Of these, half (23) have received a negative reimbursement decision, while the other half are either under evaluation or reimbursement has not yet been requested.



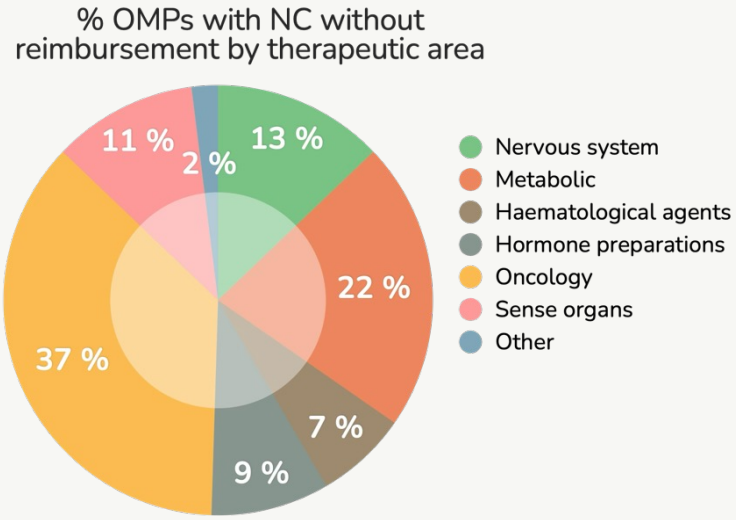
Of these 46 orphan medicines:

- Thirty-five percent (16) have been waiting for public reimbursement since 2015-2020.
- Twenty-two percent (10) with NC in the 2021-2023 period remain non-reimbursed by the NHS.
- The remaining 43% (20) received NC in 2024.

In addition, as shown in the graph below, almost 40% of the OMPs with NC but yet still to be reimbursed **have been waiting more than 3 years for their incorporation into the NHS**, although it is true that more than 40% (20) have been in this situation for less than a year.



Of the non-reimbursed orphan medicines, 37% are oncological and 22% for metabolic diseases, among others.



The Annual Report also includes information on CIPM meetings that have considered these medicines, and the criteria agreed upon to deny their reimbursement (information reflected in the minutes published as of 31 December 2024 available on the web page of the Ministry of Health).

Of these 46 orphan medicines, 17 have gone through the CIPM during the 2018-2024 period. For 16 of them, the **agreed criteria for refusing their reimbursement** was reflected**, and in all of these, criterion d** - rationalisation of expenditure - **is included** for non-reimbursement. On the other hand, **criterion c** - therapeutic and social value - has been included in decisions for 6 medicines and, finally, **criterion e** - existence of other alternatives at a lower price - for 3.

On the 20 OMPs not funded with **NC from 2024**, only 1 has gone through the CIPM, and reimbursement was rejected due to **criterion d**.

09 KEY RESULTS

01 For AELMHU, the data on access to orphan medicines in 2024 continue to reflect that the future of orphan treatments in the EU remains positive, which represents **extraordinary news for all those patients and families** who have not yet found a diagnosis or treatment for their pathologies and look to pharmaceutical innovation with great hope. However, as we mentioned in the Introduction, it should not be forgotten that only the 6% of rare diseases have treatment, so we must continue to maintain and increase, among all of us, the effort to increase this percentage.

02 The figures at the European level are positive, since **all the Community indicators have improved** in the last year**, albeit unevenly**. The 25 new orphan designations is a relatively high figure compared to other years, although the number of marketing authorisations (17) is lower. Even so, this is an important result, and we need to monitor these two indicators in the short term, with the aim of maintaining and increasing these figures over the next few years.

03 Spain has achieved a **historic increase in new National Codes (24)**, which has reduced the percentage of orphan medicines with MA, but without NC, by 5 percentage points. In addition, **the increase in the number of new OMPs reimbursed by the NHS (17) has been considerable**, although all but one of these medicines had to be considered at least twice by the CIPM to obtain a positive resolution. This proportion is higher than in 2023.

04 The **waiting time** between NC and positive reimbursement position, however, **has remained at 23 months**, so that the downward trend observed in 2023 has not continued. In this sense, we must all work together to reduce access times, so that it becomes a key objective to be pursued with the expected regulatory development, both in Europe and in Spain, given that at present we are still far from meeting the timelines included in the current legislation.

05 In terms of reimbursement, the percentage of orphan medicines reimbursed by the NHS with respect to the total number of European authorisations continues to rise, reaching 58% (from 53% in 2023), so that **Spain** now **reimburses (almost) 6 out of every 10 orphan medicines approved by the EU**. In addition, it is worth mentioning that 3 of the treatments reimbursed in 2024 obtained their NC that same year, so that their waiting times have been relatively short. It is worth remembering that none of the 10 treatments that obtained NC during 2023 were reimbursed during that same year.

06 All new products reimbursed during 2024 continue to **have conditional reimbursement and follow-up conditions**, and, in addition, a slightly higher proportion than last year has restricted reimbursement (based on EMA-approved indications). **There has also been an increase in the proportion of OMPs (all but one) subject to 2 or more reimbursement conditions**.

07 On the other hand, as of 31 December 2024, **there were 16 OMPs approved at the European level that did not have a National Code in Spain**, representing 11% of the total number of those authorised. We observe a considerable reduction in this indicator, so we believe it is important to continue this path. However, of these, 87% have been authorised for more than one year and have not yet reached our market, which means that there is less availability of relevant innovations for Spanish patients.

08 There were 15 advanced therapies with orphan designation and marketing authorisation by the end of 2024. While 14 of these have National Code, only half are reimbursed by the NHS - and **3 of these 7 have been reimbursed in 2024**, an important milestone that had not occurred since 2021. Of the remaining 7 therapies with NC, but not reimbursed, 5 have an unfavourable resolution, and 2 are under evaluation or without request for reimbursement.

09 At present, **46 orphan medicines are not reimbursed in Spain**, 1 more than in 2023, and almost 40% have been waiting more than 3 years for their incorporation into the NHS. The main reasons for not reimbursing have been the rationalisation of public spending and the therapeutic and social value of the medicine.

10 ASSESSMENT AND RECOMMENDATIONS

01 This new edition of the Annual Report on Access to Orphan Medicinal Products in Spain aims to continue providing information on the current and historical situation of the access to these treatments in Spain. The objective is to continue the dialogue with all the agents in the sector, to improve patients' access to the treatments that, unfortunately, so desperately need.

02 Access data for the year 2024 show positive and encouraging results, especially in terms of orphan medicines with a National Code. It is necessary to continue reducing the percentage of OMPs authorised in Europe, but which do not reach Spain, and not returning to the figures of previous years. In 2019 the percentage was 9%, and an aspiration for 2025 would be to reduce it below this figure. The number of medicines reimbursed by the NHS has also seen a significant increase, and **Spain reimburses almost 6 out of every 10 orphan medicines with a European Marketing Authorisation (MA).**

03 **Waiting** times between the National Code (NC) and its inclusion in the NHS, however, remained the same as the previous year. As good news, 3 of the medicines reimbursed in 2024 obtained their NC that same year (no medicine with NC in 2023 was reimbursed that same year). Providing treatments to patients in a timely manner, including those newly authorised, requires an effort from everyone and it is imperative to continue working on shortening these timelines. To this end, AELMHU expresses our members' **commitment** to work collaboratively among all stakeholders, in a trusted environment.

04 This context leads us to demand, once again, that Spain should be able to **improve and speed up the approval processes for OMPs**, especially since their efficacy and safety has already been accredited by the European Medicines Agency (EMA).

05 Orphan medicines provide important health value for patients with rare diseases, but also economic and social value for Spain, as AELMHU has been defending for many years, based on the conviction that **innovation is a tangible asset for society as a whole and should be a national priority**.

06 In terms of legislative matters related to access, 2025 is expected to be an important year. At the European level, we already have in place the European Health Technology Assessment Regulation, which will be of particular importance for orphan medicines. This new process **will evaluate eligible medicines from a clinical perspective** (through Joint Clinical Assessments), which include the following four domains: the identification of a health problem and the current health technology, the analysis of the technical characteristics of the new health technology, its relative safety and its relative clinical efficacy. What is important at the national level is that the result of the evaluation should be factored in when evaluating the non-clinical domains in Spain, including economic evaluation, and ethical, organisational, social and legal aspects.

07 There have also been new developments in Spain. Firstly, in August 2024, **the draft Royal Decree regulating the evaluation of health technologies** was published. **In December 2024, the public consultation prior to the draft Royal Decree regulating the procedures for the reimbursement and pricing of medicines was published**. AELMHU submitted contributions to both consultations. What has not yet been published is the Preliminary Draft of the Law on Medicines and Medical Devices.

08 As stated in our contributions to the Draft Royal Decree on evaluation, from AELMHU we want to thank our inclusion in the Regulatory Impact Report of this Draft, as part of the group of organisations that should be heard in their contributions in this hearing process, and we value positively these advances in regulatory matters. However, **we consider that this Royal Decree should recognise the specificities of the special characteristics of rare and ultra-rare diseases**, in line with Regulation (EU) 2021/2282, on health technology assessment, and other EU reference policies. The inherent characteristics of rare and ultra-rare diseases require a specific approach in the evaluation of medicines aimed at them. This specific approach is well established in other countries, as well as at the European level. For this reason, we consider it essential that the new evaluation system includes a specific process for orphan medicines, with evaluation criteria in line with the characteristics of these medicines. In last year's Executive Summary, we already mentioned that AELMHU had shared two documents with the Ministry of Health, one with recommendations on possible reforms for the access and evaluation process of orphan medicines, and the other on an "Early Access" program for medicines with orphan designation or medicines for minority diseases. These two documents served as the basis for our input to the relevant consultations.

09 With regard to the public consultation prior to the draft Royal Decree on prices, our contribution highlighted that **at AELMHU we are committed to reaching the greatest possible consensus**, among all the agents involved, with the necessary provision of resources to the system, ensuring holistic governance and guaranteeing Spanish healthcare regulations takes a social perspective. We also consider it essential to **implement governance mechanisms and instruments** that facilitate the joint and consensual development of innovation assessment models, adapted to each pathology. In this public consultation, reference is made to procedures and conditions for **accelerated, conditional and provisional reimbursement** authorisations, something not currently contemplated in our system. AELMHU has been working along these lines for years, as reinforced by our recommendations for an "Early AccessÓ program in Spain for medicines with orphan designation or medicines for rare diseases. Other suggestions we included in our contributions were:

a. The evaluation of the efficiency of medicines should be governed by a flexible framework using evaluation methodologies that value the social contribution of the medicine, as well as taking into account the specific idiosyncrasies of orphan medicines (low prevalence, limitations in epidemiological studies, and lack of comparators, among others).

b. The need to establish and strengthen a process of early and continuous dialogue between the Administration and the companies, which allows identifying emerging therapies in advance, generating the necessary evidence to facilitate access, and aligning expectations.

c. To facilitate the collection of real-world and medicine effectiveness data in the clinical practice of the Centres, Services and Reference Units of the NHS (CSURs), and to be able to use the real-world evidence generated in Spain through compassionate use/special situations.

d. Not include orphan medicines in the reference price system.

e. Include in the definitions of transparency and confidentiality those aspects that, due to the very nature of the procedure in question, must remain confidential, to safeguard competition and the correct functioning of the market, thus being in line with the objectives of the Pharmaceutical Industry Strategy.

10 On the other hand, at the end of 2024 the **Pharmaceutical Industry Strategy 2024-2028** was officially presented in our country, which has access to medicines as one of the three main pillars, with the promotion of research, innovation and development, and ensuring the competitiveness, resilience and eco-sustainability of the industrial ecosystem and its supply chains, the other two. **AELMHU was included as one of the main associations of the pharmaceutical industry in Spain**, and we have already participated in the first meeting of the so-called Mixed Ministries-Industry Committee, whose main functions are inter-ministerial coordination and monitoring of the Strategy itself, in coordination with the pharmaceutical industry. It is also important to highlight that **rare diseases, advanced therapy medicinal products and chronicity have been identified as three strategic therapeutic areas**. For 2025, it will be key for the expected regulatory reforms to take into account the objectives of this Strategy.

11 The factors that ultimately determine whether patients suffering from a rare disease have access to an orphan medicine are multiple and complex. The improvement in several indicators is undeniable, but **it is necessary to continue working in many aspects, such as the recognition of the economic and social value of pharmaceutical research on new products and indications, equity in access to these treatments, streamlining bureaucratic processes, improving the evaluation process, and greater certainty, transparency and participation throughout the evaluation and approval process, among other issues**. We hope that the important and long-awaited regulatory developments in 2025 will take all these aspects into account.

12 As a final comment, and beyond the figures included in the Report, it is imperative to **ensure equity in patient access to orphan medicines between different Autonomous Communities.**

AELMHU wants to reiterate its invitation so that all together -industry, patients, scientific community, professionals and public decision-makers- **join forces to find solutions that improve the quality of life of all those who suffer from a rare disease**.

We hope to continue to report good news in our 2025 quarterly reports.

11 SOURCES OF INFORMATION

01 Medicinal products with positive orphan designation from the European Medicines Agency

02 Community Register of Orphan Medicinal Products

03 Orphan Medicinal Products authorised by the AEMPS

04 Orphan Medicinal Products reimbursed by the NHS (Nomenclature)

05 Interministerial Medicine Pricing Commission (CIPM) Agreements

12 ACRONYMS

- **AEMPS:** Spanish Agency of Medicines and Health Products.
- **ATMPS:** Advanced Therapy Medicinal Products.
- **CHMP:** Committee for Medicinal Products for Human Use.
- **CIPM:** Interministerial Medicines Pricing Commission.
- **COMP:** Committee for Orphan Medicinal Products.
- **EMA:** European Medicines Agency.
- **EU:** European Union.
- **MA:** Marketing Authorisation.
- **NC:** National Code.
- **NHS:** National Health System.
- **OD:** Orphan Designation.
- **OMP:** Orphan Medicinal Product.
- **REER:** State Registry of Rare Diseases.

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