European Rare Diseases
Research Alliance

Resource on the State of the Art of Rare Disease Activities

2025 Report for Spain

National Mirror Group

Spain has a National Mirror Group (NMG), which was launched on 10th June 2025. The NMG is coordinated by the Institute for Rare Disease Research. This NMG has overseen the collection of data from Spain via a data contributing committee. Contributors are listed at the end of this report.

Definition of a Rare Disease

Spain adopts the formal European Union (EU) definition of a rare disease (i.e. those with a prevalence of no more than 5 patients per 10,000 persons. This definition is laid down in Regulation EC no. 141/2000 on Orphan Medicinal Products, Directive 2011/24/EU on Cross Border Healthcare as well as in the Council Recommendation on an action in the field of rare diseases of 8 June 2009.). The National Strategy does not espouse this definition but it is used throughout Spain.

Status Quo of any National Plan or Strategy for Rare Disease

What is the status quo?

Spain has a National Strategy for Rare Disease that is described as open-ended and live. The initial National Strategy for Rare Diseases (2009) was time-bound, with a first implementation period, later updated in 2014. However, the Strategy has since been maintained as an open-ended framework, remaining in force whilst the latest edition (2025) is being developed. The new strategy will have a results-oriented approach, continuous monitoring, and alignment with the forthcoming European Action Plan for Rare Diseases 2025–2029. Further information is available here.

In 2024, a formal evaluation of the strategy was carried out, identifying areas for improvement (particularly regarding territorial equity, care coordination, and the promotion of research). The evaluation did also highlight significant progress achieved.

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Elaboration and Adoption/How was the original strategy elaborated?

Spain adopted its first National Strategy for Rare Disease in 2009, which was later updated in 2014 within the framework of the National Health System (NHS) Strategies. Its development and adoption followed a participatory process coordinated by the Ministry of Health, involving Autonomous Communities, scientific societies, patient organisations, and subject-matter experts. The Strategy was approved by consensus through the Interterritorial Council of the National Health System (CISNS), giving it official status. Although the strategy is not enshrined in law or regulation, it does form part of the strategic planning of the NHS.

A dedicated group was in charge of overseeing the drafting and adoption of Spain's National Strategy for Rare Disease. This multidisciplinary working group included the following stakeholder types:

- Patients/people with lived experience of rare condition
- Spain's National Alliance of Rare Disease patient organisations
- Health Ministry/Competent National Authority in charge of Health or Care
- Research Ministry/ Competent National Authority in charge of Research
- Education Ministry/ Competent National Authority in charge of Education
- Social or Welfare Ministry/ Competent National Authority in charge of social affairs
- Research funders
- Researchers/clinicians from rare disease centres
- ERN coordinators or representatives
- Autonomous Communities

The drafting and adoption of the National Strategy for Rare Diseases (Estrategia en Enfermedades Raras del SNS) is coordinated by the Ministry of Health, through the General Sub-Directorate for Quality of Care. In addition, the Strategy is supported by a group of scientific coordinators, composed of national experts in rare diseases, who contribute to the technical and scientific development of the document. It also relies on an Institutional Committee, comprising of representatives from the 17 Autonomous Communities and two Autonomous Cities of Spain, and a Technical Committee, which brings together patient associations, scientific societies, professional forums, and related platforms. Together, these bodies ensure that the Strategy reflects the perspectives of all relevant stakeholders and maintains both scientific and territorial coherence.

Is there funding for the Plan? How is it Implemented and/or Monitored or Evaluated?

Spain's National Strategy for Rare Disease has a dedicated budget. Since 2021, an annual allocation of €1,409,035 has been provided by the Spanish Ministry of Health to support the implementation of the strategy. In addition to this central funding, each Autonomous Community contributes its own resources to finance specific projects aligned with the strategy's objectives. Furthermore, a dedicated budget of €1,000,000 is allocated annually to the National Rare Disease Registry (ReeR), supporting the collection, management, and analysis of epidemiological data at the national level.

The same group responsible for drafting/adopting the national strategy is responsible for implementing and overseeing the strategy. The group meets occasionally but irregularly. Formal and comprehensive evaluation and monitoring takes place for Spain's National Strategy for Rare Disease. The evaluation and monitoring of the National Strategy for Rare Diseases is coordinated by the Ministry of Health,

through the General Sub-Directorate for Quality of Care, in close collaboration with the Institutional Committee (representatives from all Autonomous Communities) and the Technical Committee (scientific societies, patient organizations, and experts). These groups jointly review progress, identify areas for improvement, and propose updates to ensure alignment with national priorities and the evolving landscape of rare diseases.

Research in National Plans or national research strategies relevant to rare disease

Spain's national strategy for rare disease does address rare disease research. Research related activities included within the plan are supported financially. The national strategy includes references to rare disease research initiatives such as IRDiRC and COST (Cooperation in Science and Technology) actions. The national strategy addresses the following topics relating to rare disease research:

- Registries or registry catalogues for rare diseases
- Biobanks/biosample catalogues for rare diseases
- Ontologies, codification or data standardisation
- Clinical/Translational research
- Sociological (e.g. Quality-of-Life-related) or socio-economic research

Each national health strategy in Spain has its own dedicated committees to ensure focused governance and coordination. In the case of the National Strategy for Rare Diseases, the implementation and oversight structure (composed of the Institutional Committee, Technical Committee, and the group of scientific coordinators) is specifically dedicated to this Strategy. Nevertheless, its execution is understood as a shared responsibility across the National Health System, requiring broad participation and dissemination among regional health authorities, healthcare professionals, researchers, and patient organisations to ensure the effective translation of the strategy's objectives into practice nationwide. In addition to these specific committees, the implementation of the National Strategy for Rare Diseases is considered a shared responsibility across all levels of the health system. It is not limited to a single representative or unit within each Autonomous Community but rather requires broad dissemination and active involvement from multiple actors including regional health authorities, healthcare professionals, researchers, and patient organisations.

The National Strategy for Rare Diseases in Spain is closely aligned with other national health strategies, particularly the National Strategy for Neurodegenerative Diseases (including ALS) and the Chronic Disease Strategy. This alignment ensures a coordinated approach to improve prevention, early diagnosis, comprehensive care, and social support for patients with complex and long-term conditions.

Spain's National Strategy on Rare Diseases is developed within a broad framework of international cooperation and shared learning. Whilst it is grounded in Spain's national health system, it has been informed by the principles and recommendations of the European Union, the World Health Organization (WHO), and by the experiences of other partner countries.

Spain, together with Egypt, led the drafting and adoption of the WHO Resolution on 'Rare Diseases: a Global Health Priority for Equity and Inclusion', which was approved in May 2025. This resolution reinforces the need for coordinated global action and aligns closely with the objectives of Spain's national policies. In practice, Spain contributes to and benefits from international collaboration through several mechanisms. Spain plays an active role in the European Reference Networks (ERNs). Beyond

Europe, Spain also cooperates with Ibero-American countries through platforms such as ALIBER (Ibero-American Alliance for Rare Diseases) and RIBERSER, supporting joint initiatives in research, training, and patient empowerment. Whilst Spain's National Strategy is implemented at the national level, its design, evaluation, and evolution are closely linked to the international commitments and partnerships that Spain actively promotes within the WHO framework and beyond.

Select Achievements of the National Plan

Below are five select achievements resulting from Spain's National Strategy for Rare Disease:

1. Creation and ongoing development of the National Rare Disease Registry (ReeR), which compiles epidemiological data to support planning, research, and health policy decisions.
2. Designation and consolidation of Reference Centres (CSURs) for rare diseases, ensuring equitable access to specialised and high-quality care across the country.
3. Development of training and awareness programs for healthcare professionals to improve early diagnosis and multidisciplinary management of rare conditions.
4. Strengthened collaboration with patient organizations, particularly through structured engagement with the Spanish Federation of Rare Diseases (FEDER) in policy design and implementation.
5. An annual allocation of national and regional funding supports the implementation of projects under the Strategy, focusing on enhancing social and healthcare coordination through case management models, strengthening neonatal screening programs, and developing training and information initiatives for healthcare professionals, patients, and families to improve knowledge, communication, and the overall quality of care for people living with rare diseases.

Rare Disease Research Programmes and Funding

Spain has specific research programmes/funding calls dedicated to rare disease research, which are offered regularly by both public and private bodies. The bodies who fund rare disease research in Spain include the Spanish Federation of Rare Diseases (FEDER) and The Carlos III Health Institute (ISCIII) through the Strategic Action in Health (AES), within the framework of the Spanish State Plan for Scientific, Technical and Innovation Research. The approximate value of national investment in Spain in rare disease research through programmes/funding calls in the past five years is over €148 million. It is expected that there will be further funding allocated to rare disease research programmes/funding calls, following the World Health Organisation (WHO) resolution recommendations.

Rare Disease Registration and Biobanking

There is a national rare disease registry for rare disease in Spain called the Carlos III Health Institute (ISCIII) Rare Disease Patient Registry (RePER). Both professional and patients can participate within the registry. Professional research societies or groups involved in the registry sign a collaboration agreement with the Rare Diseases Research Institute (IIER) and the ISCIII. The data model is defined in collaboration with those responsible, maintaining interoperability between patient records. The

informed consent form, which has been evaluated and accepted by the IIER Ethics Committee, is provided. The registry is registered with the Spanish Data Protection Agency, so any registry that is integrated into it does not need to make its own declaration. There are different permissions so that each group will only have access to the information of the patients in its registry. Access for research projects requires an evaluation from the Ethics Committee. The RePER registry embeds FAIR (Findable, Accessible, Interoperable, Reusable) data principles. The registry uses Orphacode, OMIM (Online Mendelian Inheritance in Man) and ICD10 coding systems. The registry collects the Common Data Elements for rare disease registries, recommended by the European Commission, through the European Platform on Rare Disease Registration (EU RD Platform). There is another national registry for 33 rare diseases, at a population-based level, which is managed by the ISCIII-IIER and it is populated by autonomous communities (Spanish regions) from healthcare data and statistics.

Spain does have disease specific rare disease registries, and some are included within RePER.

Spain has a national biobank specifically for the collection for rare disease biosamples. The metadata for the biobank is available in the BBMRI (Eurobiobank), RD-Connect and Solve-RD.

Organisation of Rare Disease Care

Centres of Expertise

There is a national policy in place for designating rare diseases Centres of Expertise in Spain. There are centres both at the cross-rare disease level and for specific rare diseases. Spain has 334 CSUR (Reference Centres, Services and Units) in 52 centres for the treatment of a total of 101 rare or complex diseases. Centres must meet the criteria below to apply for designation:

- Proven sufficient knowledge and experience in the management of the pathology, technique, technology, or procedure in question.
- Have had or anticipate sufficient activity in the technique, technology, or procedure for which designation as a reference centre, service, or unit is sought to ensure an adequate level of quality and safety for patients.
- Have the necessary equipment and personnel to carry out the activity in question.
- Have the resources required for adequate patient care available, in addition to those of the reference service or unit itself.
- Obtain adequate performance indicators prior to designation.
- Have an information system in place that allows for knowledge of the activity and evaluation of the quality of the services provided.
- Have the capacity to train other professionals in the activity designated as a reference.

A designation committee is in place, and they can propose additional criteria according to the type of condition.

ERNs

Spain is involved in multiple European Reference Networks. For the latest details on participating HCPs, click here.

In addition, two of the 24 ERNs are coordinated by a Spanish centre:

EpiCARE	Hospital Infantil Sant Joan de Déu, Barcelona	Professor Alexis Arzimanoglou
ERN TransIplantChild	Hospital Universitario La Paz, Madrid	Dr. Paloma Jara Vega

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Newborn Screening

At a national level, 23 conditions are included in Spain's newborn screening programme. Different regions within Spain can screen for more conditions. Further information can be found here. The Ministry of Health and Consejo Interterritorial de Salud (Council that includes the 17 Autonomous Communities and 2 Autonomous Cities) decides the common minimum care for all regions. Usually a Health Technology Assessment (HTA) is conducted to evaluate the screenings (i.e. cost-effectiveness).

Diagnostics

In Spain, genetic testing is carried out in public reference laboratories, in health care settings. A basic portfolio of genetic testing is in included in the public provision of healthcare.

Genetic testing for undiagnosed patients/people with currently undiagnosable conditions is carried out through the Spanish Undiagnosed Rare Diseases Program (SpainUDP) at ISCIII-IIER and through other UDP programs, as well as the national initiative called IMPACT Genomica.

There is a policy in place in Spain to ensure national providers provide genetic counselling for patients with a suspected or confirmed rare disease. This is carried out a national level but each region in Spain may have additional regulations.

National Alliances of Rare Disease Patient Organisations

Spain has a national alliance of rare disease patient organisations called Federación Española de Enfermedades Raras (FEDER). Further information can be found here. FEDER is involved Spain's National Mirror Group (NMG) and in setting the strategic direction for rare disease research within Spain.

In Spain, FEDER works closely with leading research consortia to promote research into rare diseases: ISCIII, IIER, CIBERER, and CSIC, as well as with representatives from the Ministry of Science, Innovation, and universities. Furthermore, FEDER advocates for the research needs of their community at meetings, conferences, and events where various stakeholders are represented, including national and regional government. At the European level, FEDER participates in technical meetings with Rare Disease International, EURORDIS, amongst other organisations.

The FEDER Foundation is committed to scientific dissemination and biomedical training for its members. One of its initiatives is the publication of the Research Notebooks, a series of thematic booklets that aim to present bio-clinical, scientific, and other concepts and topics in a simple and schematic way. Further information can be found here. FEDER also conducts webinars and training courses on different topics to educate, inform, and update their associative movement.

FEDER has carried out a project to identify the research investment made by their associative movement during the three-year period 2021-2023. This was made possible by conducting interviews with more than 190 entities known to fund research. A report has been published that highlights the important role of patient advocacy groups in research into their diseases and the need to continue supporting research into rare diseases.

FEDER have identified several barriers that might prevent or restrict patient engagement in rare disease research. Associations need professional support to get started in the research process. It's difficult to secure funding, identify research teams with expertise in their specific pathology, write research proposals, and obtain support in translating and understanding scientific publications, among other things.

Information Resources for Rare Disease

National Orphanet Engagement

Spain has an operational Orphanet team hosted by Consorcio Centro de Investigación Biomédica en Red (CIBER). The Orphanet-Spain team is mainly funded by the hosting institution and through funds linked to European projects. The team regularly searches for national resources to be registered within the Orphanet database. The main resources included in the database are expert centres, research projects, clinical trials, patient organisations, registries and biobanks. For further information regarding the procedures and information sources used, click here.

Helplines

Spain has national information portals/helplines dedicated to rare disease available for anyone to use and are supported by a mixture of public and private funding. Information is provided via the Spanish rare disease registry (RePER). Spain's National Alliance (FEDER) provides information and support to patients via their website, emails and by phone.

Training and Education

There are rare disease training activities within Spain. Training activities in Spain are provided by academia, research Institutions (e.g. IIER-Instituto de Investigación en Enfermedades Raras, CIBER-RD Area, RER-CSIC), medical and scientific societies, university hospitals, patients organisations and Orphanet-Spain. Training is provided on the following topics:

- Diagnostics
- Awareness of rare disease
- Data management
- Data quality
- FAIR data
- Standards and quality of genetics/genomics data in clinical practice and laboratories
- Registries
- Biobanks
- PPIE
- Clinical research

A recent analysis on rare disease training activities in Spain, carried out in preparation for the update of the National Rare Disease Strategy, reached the following conclusions:

- Professionals:
  - There are continuing education courses on rare disease for medical, nursing, and biosanitary professionals, although they are fragmented and not mandatory.
  - 20% of university curricula (across seven Spanish universities) include specific courses on rare disease and/or clinical genetics.
- Undergraduate Academics:
  - In the field of Medicine, seven Spanish universities offer a required or elective course in undergraduate clinical training in rare diseases and/or clinical genetics.
  - In the field of Biology (Biomedical Sciences, Biotechnology, etc.), there is adequate training in human genetics. However, there is a lack of training specifically focused on all of the biological and pathophysiological aspects of interest in rare diseases.
- Citizenship:
  - Low social awareness: 60% of people in Spain are unaware of what rare diseases are (FEDER Study, 2023).
  - Lack of accessible, easy-to-read materials for patients and families.
  - Specific needs identified in some areas, such as therapies in specific aspects like outpatient management of treatments.

Orphan Medicinal Products (OMPs)

The Spanish Association of Orphan and Ultra-Orphan Medicines Laboratories (AELMHU) publishes two key reports for monitoring the OMPs ecosystem in Spain, on access to OMPs and clinical trials for rare diseases respectively. Both are compiled using publicly available data from the European Medicines Agency (EMA), the Ministry of Health and official registers, and are updated every four months and annually.

AELMHU's Access Report has become the key reference to ascertain both the number of OMPs available and with a reimbursement decision in Spain, and their timelines. The latest quarterly Access Report was published in September 2025, with data up to the 31st August. Of the 156 medicines with orphan designation and marketing authorisation in the EU available at that time, the key results for Spain are as follows:

- 135 OMPs have an assigned National Code
- 104 of them are reimbursed by the National Health System (67% of those with marketing authorisation).
- Of the 104 reimbursed OMPs, 58% are funded with restrictions, either due to restrictions on authorised indications or because they have an indication not reimbursed.
- Moreover, all OMPs reimbursed during 2025 so far are subject to financing conditions.
- 21 OMPs with EU marketing authorisation (13%) do not have a National Code, and hence are pending arrival in Spain to begin with their pricing and reimbursement process.
- The average time between the assignment of the National Code and incorporation into the NHS is 24 months in 2025, one month longer than the average time in 2024.
- It is important to highlight that the number of OMPs available in Spain has shown a positive trend over the last two years.

The data collected in this report refers exclusively to national access, as Spain has a decentralised National Health System made up of 17 Autonomous Communities (and 2 Autonomous Cities), for which there is no public and homogeneous information on effective access at the regional level. This limitation prevents from identifying possible territorial differences in the actual availability of treatments. OMPs available via expanded access programmes are also not included in the report Access Report. For further information, click here.

Historically, the Spanish healthcare system has two relatively well-established regulated channels that allow early or expanded access to medicines, even before their formal authorisation or effective marketing, which are particularly relevant in the field of rare diseases.

This access is articulated through the regulatory framework established by Royal Decree 1015/2009 of 19 June, which regulates the availability of medicines in special situations ("medicamentos en situaciones especiales") and provides for two main mechanisms:

1. **Compassionate use:** managed by the Spanish Agency for Medicines and Health Products (AEMPS), which allows individualised access to unauthorised medicines for patients with serious or rare diseases without available therapeutic alternatives. This procedure is activated

at the request of the responsible healthcare professional and requires express authorisation from the AEMPS.

2. **Access in special situations:** applicable to medicines already authorised by the European Medicines Agency (EMA) but not yet marketed or reimbursed in Spain. In these cases, access can be managed through specific programmes promoted by the marketing authorisation holders, in coordination with the competent health authorities.

Spain is currently reviewing key regulations and legislative proposals that can have a significant impact on the accessibility to OMPs. In particular, the potential introduction of an accelerated/temporary/conditional reimbursement pathway, for potentially innovative therapies and where OMPs are expected to be potential candidates for these new pathways. This would be the official 'early access' scheme potentially allowing access for patients while the standard pricing and reimbursement negotiation is taking place. AELMHU has presented a set of proposals to the Ministry of Health to support the implementation of this new pathway.

Farmaindustria has actively contributed by submitting comments and proposals on draft regulations to review national legislation. They have developed a proposal for early access to medicines (including those without therapeutic alternatives) through an accelerated funding mechanism within 90 days. Additionally, Farmaindustria participates in a joint working group under the Government's Pharmaceutical Industry Strategy, where the first focus area addresses access and sustainability, including orphan drugs.

According to AELMHU, in the field of international cooperation, Spain actively participates in various initiatives aimed at improving access to medicines and therapies for rare diseases. Of particular note is its role as one of the three co-sponsors of the resolution 'Rare diseases: a global health priority for equity and inclusion, adopted by the 78th World Health Assembly in May 2025. This resolution officially recognises rare diseases as a global public health priority and promotes equitable access to essential services such as diagnosis, treatment and clinical follow-up.

At the European level, Spain is participating in negotiations on the new European Union Pharmaceutical Legislation, which incorporates specific measures to encourage the development and availability of orphan medicines. This regulatory alignment seeks to strengthen a national and international ecosystem that facilitates access to innovative therapies, especially in priority areas such as rare diseases.

Spain is also involved in key European initiatives such as the European Rare Diseases Platform (EU-RD Platform), which focuses on the harmonisation of data and registries, and is also represented on the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA), the body responsible for evaluating applications for orphan drug designation and advising on applicable regulatory incentives.

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The Data Contributing Committee of Spain, which provided this 2025 data (correct as of the end of November 2025) in the context of the Resource on the State of the Art of Rare Disease Activities, is composed of representatives from the following organisations:

- Beatriz Arconada, Spanish Federation of Rare Diseases (FEDER)
- Carla Dueñas, Coordinator Strategy for Rare Diseases (Ministry of Health)
- Virginia Corrochano, Orphanet Spain
- Marian Corral, Spanish Association of Orphan and Ultra-Orphan Medicines Laboratories (AELMHU)
- Amelia Martín, Farmaindustria
- Rodrigo Sarmiento, María Sánchez, Verónica Alonso & Eva Bermejo-ISCIII-IIER Team