State of the Art of Rare Disease - Activities in EU Member States and Other European Countries

Portugal Report

Definition of a Rare Disease

Portugal has adopted the European Commission definition of a rare disease and the national plan espouses this definition.

National Plan/Strategy

Portugal has adopted a National Strategy for rare diseases. There is a policy decision in place to ensure long term funding and sustainability of the measures within the national strategy.

A dedicated body exists to oversee the drafting and implementation of the National Strategy, it is multi-stakeholder (including patients) and meets on a regular basis.

The Strategy is coordinated by an interministerial commission, presided over by the Director-General of Health, which sets out its functioning rules. It is composed of the following members:

- One representative of the Directorate-General of Health;
- One representative of the National Institute of Health, Dr. Ricardo Jorge, I. P.;
- One representative of the Central Administration of the Health System, I.P.;
- One representative of the National Authority for Medication and Health Products, I.P.;
- One representative of the Social Security Institute, I.P.;
- One representative of the National Institute for Rehabilitation, I.P.;
- One representative of the Foundation for Science and Technology, I.P.;
- One representative of the Directorate-General of Education, in the area of special educational needs.

The Integrated Strategy for Rare Diseases, based on an interministerial, intersectoral and interinstitutional cooperation, which makes a complementary use of medical, social, scientific and technological resources, has as mission the development and improvement of:

- Coordination of care;
- Access to early diagnosis;
- Access to treatment;
- Clinical and epidemiological information;
- Research;
- Social integration and citizenship

Organisation of Rare Disease Health and Social Care

Centres of Expertise

Portugal has a national policy in place for the designation of Centres of Expertise for rare disease. The following is the national criteria used to designate each Centre:

- The recognition of a Reference Centre by the Ministry of Health is officialised by an order of the Government body responsible for the Health sector, published in the Official Gazette, and it shall be valid for four years.
- The Reference Centres are subject to a periodic evaluation, by an external auditing, regarding the compliance with the general and specific requirements, which were the basis of their recognition.
- The recognition of a Reference Centre shall cease by means of an order from the Government body responsible for the Health sector, published in the Official Gazette, if any of the requirements which were the basis of its recognition are no longer met.

Currently there a 6 Centres of Expertise who comply with the national policy and 6 fulfilling the EUCERD criteria.

Co-funded by
the Health Programme
of the European Union

European Reference Networks (ERNs)

In 2016 Portugal has a formal process in place for the endorsement of Health Care Providers to participate as members or coordinators of a European Reference Network. At present there are 8 HCPs participating in 16 ERNs as full members and 0 acting as coordinators.

Rare Disease Registration

Neither national nor regional rare disease registries exist in Portugal but disease specific registries are available. However, national efforts are underway for the construction of a National Rare Disease Registry.

The Ministry of Health of Portugal was recommended by the Assembly of the Republic to implement a personal card for people with rare disease in order to give them a special status in the health system. Since then, the Directorate-General of Health has made great efforts to develop this project and to involve all the stakeholders. By the end of 2013, a card for people with rare diseases was issued.

The main objectives of the card are:

- To ensure access to relevant information, to doctors and nurses on clinical data and recommendations regarding emergencies and urgencies acts
- To improve the integrated management of the disease to avoid delay, error and harmful procedures.
- To guarantee the correct referral to Reference Centres
- To improve continuity of care, between all the levels of care.

The card must be required by the medical doctor at the national Healthcare Data Platform (PDS) during a medical consultation and patients are given a copy of the issuing request including a personal code.

Patients must confirm this request at the Platform (PDS) using their personal code.

After a final validation by medical doctors (to assure that all the steps of the process are accomplished), the card is sent to patients home by post.

In 2016, cards are being issued by 14 different hospitals across the country.

Genetic Testing

Genetic tests, applicable to different genetic diseases in the prenatal and postnatal periods, are carried out in genetic laboratories within the National Health System (NHS). As is the case of INSA (considered the national reference laboratory), as well as in laboratories located or associated with genetic services in public hospitals, and also in private laboratories. Besides these, a certain number of universities and research institutions labs also offer genetic testing.

In cases where a genetic test is not available in Portugal, the hospital of national health system can required this to be carried outside of the country, by a formal mechanism nominate Foreign Medical Assistance. On the other hand, patients can also request a foreign test using another mechanism - the S2 model form (in case the test is available in Portugal) or by the terms of Directive 2011/24/UE. These three procedures need authorization from the Health Ministry.

In order to support the implementation of a standardized and consistent way of coding RD using Orphacodes across Europe, Orphacodes will be implemented on the Portuguese request form., Genetic testing in Portugal is regulated mainly by Law 12/2005, of January 26, 2005. This law defines, among other things, the notion of health and genetic information, the circulation of information and the intervention on human genome within the health system. It also establishes the procedure to collect and preserve biological products, for the purposes of genetic testing or research.

Between 2014 and 2015 the Law 12/2015 was regulated by the Law 131/2014, and specific laws for licencing of medical genetic laboratories and the establishment of reference expertise centres were also created.

Co-funded by
the Health Programme
of the European Union

As a member of OECD, Portugal is subject to the OECD Best Practice Guidelines for Molecular Genetic Testing, which were transposed into the national law, through the Decree131/2014 which regulate Law 12/2005; Portugal also signed and ratified the Oviedo Convention, but as yet its Additional Protocol concerning Genetic Testing for Health Purposes (2008), is currently at its final stage.

Neonatal Screening

The Portuguese Neonatal Screening Program (PNSP) started in 1979 with the purpose of detecting phenylketonuria (3,542,729 new-borns screened; birth prevalence 1:10,512) and, shortly after, for congenital hypothyroidism (3,510,587 new-borns screened; birth prevalence 1:2,968).

In 2004, the expanded neonatal screening programme was implemented in the National Institute of Health Doutor Ricardo Jorge (INSA). The Program is not mandatory, with 99.8% coverage of the Country (including Madeira and Azores islands). The neonatal screening is performed in a National Laboratory that studies approximately 90,000 samples by year.

Currently, the programme screens for the following 26 diseases:

- Congenital Hypothyroidism,
- Phenylketonuria (PKU)/ Hiperphenylalaninemia,
- Tyrosinemia Type I,
- Tyrosinemia Type II/ III,
- Maple Syrup Urine Disease (MSUD),
- Citrullinemia Type I,
- Argininosuccinic Aciduria,
- Argininemia,
- Classic Homocystinuria,
- Methionine Adenosyltransferase Deficiency (MAT deficiency),
- Propionic Aciduria (PA),
- Methylmalocic Aciduria type mut- (MMA, Mut-),
- Isovaleric Aciduria (IVA),
- 3-methylcrotonyl-CoA Carboxylase Deficiency (3-MCCD),
- Glutaric Aciduria Type I (GA I),
- Methylmalonic Aciduria type Cbl C/D (MMA, Cbl C/D),
- 3-hydroxy-3-methylglutaric Aciduria (3-HMG),
- Malonic Aciduria,
- Medium Chain AcylCoA Dehydrogenase Deficiency (MCAD),
- Very Long Chain AcylCoA Dehydrogenase Deficiency (VLCAD),
- Long Chain 3-hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)/ Trifunctional Protein Deficiency (TFP),
- Short Chain AcylCoA Dehydrogenase Deficiency (SCHAD),
- Primary Carnitine Deficiency (CUD),
- Carnitine Palmitoyl Transferase I Deficiency (CPT I),
- Carnitine Palmitoyl Transferase II Deficiency (CPT II/ CACT),
- Glutaric Aciduria Type II (MADD).

A pilot study for Cystic Fibrosis is under way, screening approximately 200,000 neonates.

<u>Guidelines and Training Activities</u>

Clinical Practice Guidelines (CPGs)

Clinical Practice Guidelines for rare disease are produced at the national level in Portugal. There is also a national policy in place for the development, adoption and implementation of CPGs.

Co-funded by
the Health Programme
of the European Union

Training and Education

In Portugal, to aid the training and education of healthcare professionals and patients, there is:

- Scientific supervision of MSc and PhD students.
- Hands-on training of medical genetics and clinical genetics laboratory trainees.
- Lecturing in pre- and postgraduate educational programmes.

TRACE RD is the Training Centre for Rare Diseases founded by Raríssimas at Casa dos Marcos in partnership with Frambu, a Norwegian Centre for Rare Disorders with EEA Grants funding in November 2014.

Since then, Trace RD has developed several training activities targeting different groups: patients; families/carers; professionals; students; volunteers and other NGO leaders.

The themes are of a very wide scope and changed according to the reported needs of different groups.

Trace RD has counted close to 1000 participants and has received national and international speakers, Currently, there is already a draft calendar for 2017 with new themes and several new partners associated to each initiative.

Information Resources for Rare Diseases

Orphanet Activities

Portugal has an operational National Orphanet team which is currently housed within the Directorate – General Health. The team has produced rare disease information in Portuguese and since the beginning of 2014 the team has achieved the following:

- An inventory and classification of rare diseases
- An encyclopaedia
- A directory of services: clinics, laboratories, research projects, registries, clinical trials, patient organisations
- An inventory of orphan drugs
- Guidelines, reports
- A newsletter

National Helplines

There is a helpline in place dedicated to rare diseases in Portugal. The helpline is funded privately and is for the use of patients only.

Raríssimas has run the helpline, Linha Rara, since 2009. It was founded with financial support from the national Directorate-General for Health. Linha Rara is integrated into the European Network of Rare Disease Help Lines.

Currently, Linha Rara is the information and support service of the Association, responding to all requests in writing within a 3 working days period, notwithstanding some immediate guidance by phone or personally.

The team is made up of health professionals and social workers and recurring to other specialized areas whenever needed, medical doctors with specialist expertise and lawyers. Linha Rara has participated in several projects promoted by the association, assuming the sensitization and information activities.

Linha Rara responds not only to requests from Portugal, but from several other Portuguese speaking countries and from Portuguese citizens living abroad. Considering foreign countries, Brazil has made the highest number of requests directly posed to Linha Rara, either by phone or email.

Linha Rara no longer has the support of public financing programs, being run with the Association annual budget and with some minor contribution of the funded projects in which the Service participates such as EEA Grants funding which has supported the new bilingual website.

Co-funded by
the Health Programme
of the European Union

Official Information Centres

There are currently no official or unofficial information centres for rare disease in Portugal.

Rare Disease Research Activities

Existence of Rare Disease Research Programmes/projects

Portugal has specific programmes or projects to fund or facilitate rare disease research. The Ministries of Education and Science, and Solidarity, Employment and Social Security are planning activities in the field of social protection and socio-economic research, in the context of the Integrated Strategy for Rare Diseases.

There is a steady country-wide interest in RD research for several decades now. This research is carried out by university-based and ministry of health sponsored groups. Intensity of the different research types: basic > translational > clinical > psycho/socio-economic. Greater effort has been put into the research of the following RD: inherited metabolic disorders, lysosomal storage disorders, hemoglobinopathies, haemophilia's and thrombophilia's, mitochondrial diseases, cystic fibrosis, disorders caused by short tandem repeat expansion, genomic (or cis-ruption) disorders, and familial amyloidotic polyneuropathy.

Participation in E-rare and International Research Initiatives

At present Portugal participates in neither E-rare nor IRDiRC.

National Alliance of Patient Organisations and Patient Representation

The Portuguese National Alliance (Aliança Portuguesa de Associações das Doenças Raras) keeps raising public awareness regarding RD, both with events that are open to the all the RD stakeholders and the general public and a media campaign on national TV, radio, and in newspapers (online and paper editions), etc. The Aliança organized a conference every year, finding partners (for instance the IBMC Research Centre, Municipalities or the i3S) in order to increase the patients, doctors and other stakeholders knowledge regarding RD. In 2015, the Aliança held the Portuguese National EUROPLAN Conference with the support of the National Parliament.

The Portuguese National Alliance (Aliança Portuguesa de Associações das Doenças Raras) currently represents 10 RD Patients Associations, therefore representing around 115 rare diseases. Nevertheless, its events are currently attended by many other RD Patients Associations. The National Alliance receives requests by many patients who still have not found a RD Patient Association that suits them.

The Portuguese National Alliance participated in the drafting and implementation of the National Integrated Strategy for Rare Diseases.

Integration of Rare Diseases to Social Policies and Services

Specific programmes and facilities exist in Portugal to support people with rare diseases. There are mechanisms in place to facilitate a multidisciplinary, holistic and continuous care provision. Social interventions for people with rare diseases are already in place powered by the National Strategy for Rare Disease.

Orphan Medicinal Products

There are 90 different orphan drugs available in Portugal which are already used in 2016 (data from NHS hospitals regarding OMPs consumption). Provided by national health system. This information is available publicly on the websites of Orphanet and INFARMED (National Medicines Agency).

Portugal has measures in place to facilitate access to Orphan Medicinal Products for patients. There are Early Access Programs and/or Special Authorizations of use (whenever the medicine's assessment and financing is not yet established) available to all products (when the required patient conditions are met). However, as all Portuguese citizens are covered by the National Health Service, there are no specific measures for orphan medicinal products, as all the medicinal products follow the same procedure. The investment of the NHS in orphan medicinal products in 2014 was around € 75 million, €83 million were spent in 2015 and around € 39 million between January and June 2016.

Co-funded by
the Health Programme
of the European Union

Portugal provides incentives to support research into, and the development of (designated or potential) Orphan Medicinal Products. Reimbursement applications are exempt from fees for all the medicinal products. Public Funding Schemes (e.g. Health Research Fund) may be applied to OMPs but are not specific for OMPs. The Scientific Advice Fee may have a reduction for specific medicinal products or companies.

One initiative to support Orphan Drugs and Rare diseases in Portugal is the Rare Disease Patient Card. It allows for the accurate monitoring of patients. The implementation of the Information System regarding clinical outcomes with specific medicinal products has been planned but has not yet been put in place. Card registration contributes secondarily to the epidemiological research of RD in Portugal.

Portugal already has a medicinal products consumption reporting network that involves all NHS Hospitals (monthly report) which allows a monthly monitoring of Orphan Drugs utilization.

A multidisciplinary working group has been studying reimbursement measures and specific approval procedures, and proposed a TVF tool in order to facilitate the assessment of these type of medicines:http://www.infarmed.pt/portal/page/portal/INFARMED/MEDICAMENTOS_USO_HUMANO/SINATS/FdD/GT7

Rare Disease Day

In 2014, anticipating the Rare Disease Day, Raríssimas and Fedra presented a photo exhibition on Rare Diseases at the European Parliament. The main invitee and speaker at the Workshop Closer than Rare at the European Parliament with the participation of the Health Commissioner, researchers and European Agencies members.

In 2015, Raríssimas promoted an Open Day at Casa dos Marcos.

In 2016, Rare Disease Day was marked by official visits of both the Health Minister and the Social Solidarity Minister, who have referred to the National Integrated Strategy on Rare Diseases has a national commitment, along with clinical and scientific community representatives.

Raríssimas has organized the VIII International Congress on Cornelia de Lange Syndrome in September 2015. It brought together patients, families and professionals from several countries, not only from Europe, but also from South America and the USA.

As a member of FEDRA, Raríssimas has hosted the 2nd Iberoamerican Conference on Rare Diseases at Casa dos Marcos, with participants from all the member countries, several national Governmental representatives and with the special solidarity of the former Portuguese First Lady and Her Majesty, the Queen of Spain.

On its turn, the Portuguese National Alliance (Aliança Portuguesa de Associações das Doenças Raras - ALiança) has hosted a conference for patients and health practitioners almost every year on the vicinity of the Rare Disease Days (2008 to 2017).

Aliança, with the support of several media companies (TV, radio) has broadcasted a spot on the subject, sometimes from scratch and others by adapting the Eurordis official one, since 2010.

Other

Much has been done to further the cause of rare diseases in Portugal, including:

- The involvement of the Ministries of Health, Education and science, and of Solidarity, Employment and Social Security was a great leap forward and really helped Portugal to put the plight of rare disease patients onto the national agenda.
- The Integrated Strategy for Rare Diseases, based on an interministerial, intersectoral and interinstitutional cooperation and the approval of the Centres of Expertise for RD are the most important initiatives since 2014.

Co-funded by
the Health Programme
of the European Union