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2012 REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE OF THE EUROPEAN UNION COMMITTEE OF EXPERTS ON RARE DISEASES

STATE OF THE ART OF RARE DISEASE ACTIVITIES IN PORTUGAL

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More information on the European Union Committee of Experts on Rare Diseases can be found at www.eucerd.eu.

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ACRONYMS

General

CAT - Committee for Advanced Therapies at EMA
CHMP - Committee for Medicinal Products for Human Use at EMA
COMP - Committee on Orphan Medicinal Products at EMA
DG - Directorate General
DG Enterprise - European Commission Directorate General Enterprise and Industry
DG Research - European Commission Directorate General Research
DG Sanco - European Commission Directorate General Health and Consumers
EC - European Commission
ECRD - European Conference on Rare Diseases
EEA - European Economic Area (Iceland, Switzerland, Norway)
EMA - European Medicines Agency
ERN - European reference network
EU - European Union
EUCERD - European Union Committee of Experts on Rare Diseases
EUROCAT - European surveillance of congenital anomalies
EUROPLAN - European Project for Rare Diseases National Plans Development
EURORDIS - European Organisation for Rare Diseases
FDA - US Food and Drug Administration
HLG - High Level Group for Health Services and Medical Care
HTA - Health Technology Assessment
IRDiRC – International Rare Diseases Research Consortium
JA - Joint Action
MA - Market Authorisation
MoH - Ministry of Health
MS - Member State
NBS - New born screening
NCA - National Competent Authorities
NHS - National Health System
PDCO - Paediatric Committee at EMA
RDTF - EC Rare Disease Task Force
WG - Working Group
WHO - World Health Organization

Pilot European Reference Networks

Dyscerne - European network of centres of expertise for dysmorphology
ECORN-CF - European centres of reference network for cystic fibrosis
Paediatric Hodgkin Lymphoma Network - Europe-wide organisation of quality controlled treatment
NEUROPED - European network of reference for rare paediatric neurological diseases
EUROHISTIONET - A reference network for Langerhans cell histiocytosis and associated syndrome in EU)
TAG - Together Against Genodermatoses – improving healthcare and social support for patients and families affected by severe genodermatoses
PAAIR - Patients' Association and Alpha-1 International Registry Network
EPNET - European Porphyria Network - providing better healthcare for patients and their families
EN-RBD -European Network of Rare Bleeding Disorders
CARE-NMD -Dissemination and Implementation of the Standards of Care for Duchenne Muscular Dystrophy in Europe project
ENERCA - European network for rare and congenital anaemia – Stage 3

GENERAL INTRODUCTION TO THE REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE OF THE EUROPEAN UNION COMMITTEE OF EXPERTS ON RARE DISEASES

The 2012 Report on the State of the Art of Rare Disease Activities in Europe was produced by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD), through the EUCERD Joint Action: Working for Rare Diseases (N° 2011 22 01), which covers a three year period (March 2012 – February 2015).

The report aims to provide an informative and descriptive overview of rare disease activities at European Union (EU) and Member State (MS) level in the field of rare diseases and orphan medicinal products up to the end of 2011. A range of stakeholders in each Member State/country have been consulted during the elaboration of the report, which has been validated as an accurate representation of activities at national level, to the best of their knowledge, by the Member State/country representatives of the European Union Committee of Experts on Rare Diseases. The reader, however, should bear in mind that the information provided is not exhaustive and is not an official position of either the European Commission, its Agencies or national health authorities.

The report is split into five parts:

Part I: Overview of rare disease activities in Europe
Part II: Key developments in the field of rare diseases in 2011
Part III: European Commission activities in the field of rare diseases
Part IV: European Medicines Agency activities and other European activities in the field of rare diseases
Part V: Activities in EU Member States and other European countries in the field of rare diseases

Each part contains a description of the methodology, sources and validation process of the entire report, and concludes with a selected bibliography and list of persons having contributed to the report.

The present document contains the information from Parts II and V of the report concerning Portugal. A list of contributors to the report and selected sources are in annex of this document. For more information about the elaboration and validation procedure for the report, please refer to the general introduction of the main report[1].

[1] http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArtRDActivities.pdf

RARE DISEASE ACTIVITIES IN PORTUGAL

Definition of a rare disease

Portugal accepts the definition of rare disease, as stated in the European Regulation on Orphan Medicinal Products, as a disease with a prevalence of no more than 5 in 10,000 inhabitants. This definition has been adopted by the National Plan for Rare Diseases.

National plan/strategy for rare diseases and related actions

In November 12, 2008 the Portuguese Minister of Health approved the National Plan for Rare Diseases (*"Programa Nacional para as Doenças Raras"*).

Its main objectives are the establishment and improvement of national measures, in order to satisfy the needs of people with rare diseases and their families *vis-à-vis* medical services and care, as well as the improvement of the quality and equity of provided healthcare to those people.

Those objectives will be achieved by establishing reference centres for rare diseases, improving the access of patients to adequate care, further improving knowledge and awareness on rare diseases, promoting innovation in the treatment of rare diseases and in the accessibility to orphan medicinal products, and finally, by ensuring cooperation at national and international levels, including EU countries and those using Portuguese as their official language.

This Plan will cover all rare diseases, though it should articulate with other prioritary national plans, namely with the National Plan for Oncologic Diseases *("Programa Nacional para as Doenças Oncológicas"*).

Besides, a specific tool is already foreseen for the identification of people with rare diseases, aiming at disclosing clinical information to medical doctors and in emergency situations.

The Directorate General of Health, together with the Office of the High Commissioner for Health, have co-funded, in a total amount of €1.9 million, during the years of 2008 to 2011, a few projects on rare diseases, which are currently being developed by several patient associations, what enabled the implementation of a number of strategies mentioned in the National Plan.

Centres of expertise

There are no officially designated centres of expertise for rare diseases in Portugal. However, the National Plan for Rare Diseases will support the creation of officially recognised "Reference Centres".

The main priority is the identification at national level of reference centres and its official recognition by the Minister of Health.

Following legislation establishing norms for access to therapies involving enzymatic diseases, the National Institute of Health (*"Instituto Nacional de Saúde Doutor Ricardo Jorge"*) created a national network of treatment centres for these diseases: this programme amounted to €32 million in 2011. A list of enzymatic diseases benefiting from free of charge treatment in public hospitals is available.

Pilot European Reference Networks

Some Portuguese institutions participate, or have participated, in the following European Reference Networks for rare diseases: DYSCERNE, ENERCA, NEUROPED and TAG.

Registries

Presently there is a total of 21 registries in Portugal: 16 are from public entities, 4 belong to scientific societies and 1 is from a private institution. In 2011 the Portuguese Registry of Paramyloidosis was officially established by Order nº 8812/2011 dated 2 June 2011.

Upon their own initiative, many patients are also included in international registries or initiatives. A few Portuguese institutions also participate, or have participated, in European registries, such as, E-IMD, TREAT-NMD, EUROCARE CF, EUROCAT, EBAR, SCNIR, CHS, SPATAX, and EUROWILSON.

Neonatal screening policy

The National Programme of Early Diagnosis (*"Programa Nacional de Diagnóstico Precoce"*) started in 1979 at the Institute of Medical Genetics, and initially, it included only the screening of the phenylketonuria. Nowadays, this neonatal screening programme covers almost 98-99% of children born in Portugal and it screens 24 inherited metabolic diseases, as well as congenital hypothyroidism. The screening is made at the Institute of Medical Genetics, the only institution performing this test in Portugal. There are 5 treatment

centres to assist patients with congenital hypothyroidism and 9 centres to assist patients with inherited metabolic diseases.

Genetic testing

Genetic testing is available for many rare disorders, though, as in other countries, there is a significant flow of genetic testing over the borders. Diagnostic tests are registered as available in Portugal for 293 genes and an estimated 328 diseases, in the Orphanet database[2].

Genetic tests are carried out by genetic laboratories within the National Health System, as for instance the National Institute for Health ("*Instituto Nacional de Saúde Doutor Ricardo Jorge"*)[3], as well as in those laboratories located or associated with the five medical genetics services in public hospitals, laboratories in other services in public hospitals (e.g., IPOs – Portuguese Institutes of Oncology) and in private labs. There is also an unknown number of labs offering genetic testing services at universities and research institutions (usually on just one or a few rare diseases). There are five main private labs in Portugal responsible together for a considerable volume of the genetic testing performed in the country.

From 2006 to 2011, in the scope of medical assistance abroad, and as regards rare diseases diagnosis or its confirmation, a total of 1702 clinical cases were sent for referral to foreign centres, 70% of which for molecular study and 30% for laboratorial testing. In 2011, the number of clinical cases sent abroad for referral amounted to 374 situations. From 2006 up to 2011 an increase of 50% has been registed. In 2011 the total expenditure supported by our National Health Service (NHS) was €400 000.

When it is necessary to have a test that is not carried out by a laboratory in Portugal, there is a formal procedure to do that test abroad. Because some public hospitals have legal autonomy, like enterprises, they have contracts with public or private laboratories to make available the exams they need for clinical care.

Genetic testing in Portugal is regulated mainly by Law n.º 12/2005, of 26 January 2005. This Law defines genetic information as the health information linked to the genetic characteristics of one or more related persons (excluding, for its purposes, identity and forensic testing, as well as somatic mutations), obtained through any means, including molecular genetic, cytogenetic, biochemical, physiological tests or imaging, and family history.

Genetic information is considered to be medical information only when used for the confirmation or exclusion of a clinical diagnosis, in prenatal or pre-implantation diagnosis or for pharmacogenetics purposes, thus excluding pre-symptomatic, carrier (for recessive diseases) and genetic susceptibility testing. Only information with immediate interest for the patient's current status of health (diagnostic and pharmacogenetic information) can be entered in general hospital records; information from pre-symptomatic, carrier, susceptibility, prenatal, pre-implantation forensic and identity testing can only be registered in records of genetic services that must keep separate files (and cannot be accessed by other professionals of the same or of other health institutions, if not involved in the care of those persons).

Diagnostic or pharmacogenetic testing follows the general principles of all other health care intervention. Carrier, pre-symptomatic and genetic susceptibility testing should be preceded by genetic counselling and written informed consent, and requested through a medical geneticist. Pre-symptomatic, susceptibility and pre-implantation diagnosis should only be performed in persons that can fully appreciate all their implications and give their consent. In case of risk for a severe, late-onset disease that has no effective treatment, any predictive testing should be preceded by a psychosocial evaluation and followed after result delivery.

Insurance companies cannot ask for a genetic test or use any kind of genetic information already available (including pedigree information) to refuse life or health insurance or establish a higher premium. Employers cannot ask for or use any kind of genetic information, even with the workers' consent, except for their health protection (in case of hazardous environments), and only if done in the context of genetic counselling and if their employment is not put at risk; the exception could be made in case of serious risk to public security or public health, in which case genetic testing should be conducted by an independent entity. No genetic testing or any kind of genetic information can be requested in case of adoption, both to the adoptees or the prospective parents. In the case of minors, genetic testing should be done only in their benefit, after written consent from their parents or legal tutors, but also procuring the minors consent.

In case of severe and untreatable diseases, with onset usually in adult life, predictive testing cannot be performed in minors; and prenatal testing should not be done just for information of the parents, but only with

[2] Information extracted from the Orphanet database (September 2011).

[3] http://www.insa.pt/sites/INSA/Portugues/AreasCientificas/Genetica/Paginas/LaboratorioDeReferencia.aspx

the aim to prevent the birth of an affected child. Termination of pregnancy is legal for genetic reasons within the first 24 weeks, and up to term in case of early lethality, e.g., anencephaly.

In case of population studies that may be representative of the whole population or groups of the population, community consent should also be obtained, in addition to the individual consent. In the first case, a specific authorisation of the National Parliament is also needed.

Collection, conservation and usage of biological samples for genetic testing should be subject to informed consent, separate for health care and biomedical research, and that must include its purposes and duration of storage. If consent for a different purpose cannot be obtained, e.g. in case of death, stored samples can be used in the context of genetic counselling, in order to enable treatment or the prevention of a genetic disease in a relative (but not to know the genetic status of other family members). Biological samples cannot be used for any commercial purposes; commercial entities cannot store or use identified or identifiable samples; if absolutely needed, coded samples can be used, if the identifying codes are kept in a public institution.

A biobank is defined as any collection of biological samples or its derivatives, previously accumulated or prospectively performed, obtained through health care provision, population screening or research, with or without any identification, and with or without a time limit. Previous authorization must be requested from the health authorities and, in case of identified or identifiable data, from the Portuguese Data Protection Authority (*"Comissão Nacional de Proteção de Dados – CNPD"*[4]), the national personal data protection agency. A biobank must have a health care or a (basic or applied) health research purpose; if communication of results can be foreseen, a medical geneticist must be involved.

The Law defines a genetic database as any register, either in an informatics support or not, containing genetic information on persons or families; if a database or a genetic registry includes any kind of family information it must be curated by a medical geneticist.

Some aspects of this Law (as licensing and quality assurance of laboratories, adoption and reimbursement of genetic tests within the national health system, and direct marketing and selling to the public) are still waiting a governmental regulatory decree since 2005.

As a member of OECD, Portugal is, however, subject to the OECD Best Practice Guidelines for Molecular Genetic Testing, and has signed and ratified the Oviedo Convention.

National alliances of patient organisations and patient representation

Portugal has two alliances on rare diseases: FEDRA – Portuguese Federation of Rare Diseases ("*Federação Portuguesa de Doenças Raras"*)[5] and APADR – Portuguese Alliance of Rare Diseases Associations (*"Aliança Portuguesa de Associações de Doenças Raras*").

In 2011, FEDRA organized a Conference on "Patients, research and health policies". FEDRA also launched in 2011 the third volume of the publication "Rare Diseases from A to Z", with the collaboration of 36 experts who have reported on around 41 rare diseases, and prefaced by the Director General of Health.

APADR was officially established in 2009, and since then, has developed several action and activities with the aim of improving Portuguese health policy in the field of rare diseases, and further raising awareness to this problem.

Patient organisations were also involved in the public discussion of the National Plan for Rare Diseases. A project has been launched by the Coordinating Commission for the Plan on Rare Diseases (*"Comissão Coordenadora do Programa Nacional das Doenças Raras"*) in order to promote regular discussions with patient organisations, especially, with a view to incorporate the needs of these patients into the National Plan.

Sources of information on rare diseases and national help lines

Orphanet activity in Portugal

Since 2003, there is a dedicated Orphanet team in Portugal, currently hosted at IBMC – Institute of Molecular and Cell Biology, Porto.

The team is in charge of collecting data on rare diseases-related services (specialised clinics, medical laboratories, ongoing research projects and clinical trials, registries and patient organisations) in the country, for entry into the Orphanet database. The Orphanet-Portugal team also created and maintains the Orphanet Portugal national website[6].

Orphanet is referenced in the National Plan for Rare Diseases as the main source of information regarding activities related to rare diseases in Portugal. Though the support to its activities was specifically

[4] Portuguese Data Protection Authority www.cnpd.pt

[5] www.fedra.pt

mentioned in the Program, the Orphanet Portugal team was relaunched and relocated, after a few years of inactivity, but received no support from the Program or other national sources until 2011.

In June 2010, plans were discussed for co-funding of Orphanet-Portugal's local activities through periodical grant calls from the Directorate General of Health, together with the partnership with the National Plan for Rare Diseases. So far, 148 abstracts were already validated and became available, increasing by more than 50% the number abstracts available in Portuguese in the Orphanet website.

An official event, with media coverage, was held on 26 February 2011 to announce the launch of the Orphanet website in Portuguese, as well as the constitution of the new Scientific Advisory Board. This took place during the conference "Rare but Equal" (*"Raros mas Iguais"*), organised by the APADR in collaboration and with the support of Orphanet-PT, with the presence of the Minister and Secretary of Health, the President of INFARMED (National Authority of Medicines and Health Products), and other health authorities.

In 2011, the Orphanet Portugal team created a Facebook page called "The Orphanet in portuguese" (*"A Orphanet em português"*), hoping that it will become a forum for discussion among all Portuguese-speaking professionals, patients and their organisations, and that it will serve to promote Orphanet in their respective countries. It has already proved useful in helping finding expert volunteers for translations/validations of disease abstracts. In addition, the national team manages a considerable number of questions and inquiries, sent by users mostly by email, requesting information or help.

Orphanet-Portugal has established several partnerships[7] with APADR and the Centre for Social Studies, of the University of Coimbra, to update a validated list of Portuguese patient associations; with ACSS (Central Administration of the Health System); with INFARMED for monthly updates of the information on approved clinical trials in the context of rare diseases and of orphan medicinal products available in the country); and with NEDR (Group for the study of rare diseases at the Portuguese Society of Internal Medicine). The final contacts were also made with FCT (Foundation for Science and Technology, the major research funding agency in Portugal), for updating lists of ongoing research projects in Portugal in the field of rare diseases ("rare disease" and the respective "ORPHA number(s)", must be entered as keywords in any new applications for projects dealing with rare diseases). Other partnerships have been entered into with the CEIC (National Ethics Committee for Clinical Research), Calouste Gulbenkian Foundation, Ordem dos Médicos (National Medical Association) and "*Ciência Viva*" (Agency for public science dissemination).

Official information centre for rare diseases

Orphanet is referenced in the National Plan for Rare Diseases as the main source of information regarding activities related to rare diseases in Portugal.

Help line

With funding from the Directorate-General of Health, a call centre was implemented in 2009. The patient organisation RARÍSSIMAS was funded by the Directorate-General of Health in 2008. This help line called "Rare Line" ("*Linha Rara*")[8] received almost 2000 information requests (69% by email) in 2011.

The Portuguese Haemophilia Association also provides some support by phone. Several other patient associations have a helpline or provide help online or by email.

The Orphanet-Portugal team also deals with many requests for information from patients coming Portuguese-speaking countries.

Other sources of information on rare diseases

The APPDH – Portuguese Association of Parents and Patients with haemoglobinopathies "*APPDH - Associação Portuguesa de Pais e Doentes com Hemoglobinopatias*"), member of *APADR*, published 3 mini-books about haemoglobinopathies, mainly for children, but also useful for adults.

The APN – Portuguese Association of Neuromuscular Diseases (*"Associação Portuguesa de Doenças Neuromusculares"*) a member of APADR as well, published, in 2011, 2 booklets: "Neuromuscular Diseases Manual: for healthcare professionals" ("*Manual sobre Doenças Neuromusculares: Técnicos e Profissionais de Saúde*") and "Neuromuscular Diseases Manual: for patients and caregivers" ("*Manual sobre Doenças Neuromusculares em Idade Pediátrica: Doentes e Cuidadores"*).

[7] An updated list of all partnerships can be consulted at www.orpha.net/national/PT-PT/index/parcerias.

[8] www.linharara.pt

Good practice guidelines

Although this is the formal role of the Portuguese Medical Association ("*Ordem dos Médicos*"), the tradition in Portugal has been mainly to follow well-established and internationally respected best practice guidelines, rather than developing new ones, except for some specific contexts (as is the case with protocol for presymptomatic testing and genetic counselling in late-onset neurological disorders or some metabolic hereditary diseases).

The national coordinator of Orphanet-Portugal has been a participant and member of the steering group of EuroGentest (and EuroGentest2), a EU-funded Network of Excellence, which has developed guidelines and supports the certification and/or accreditation of genetic laboratories, and has taken important steps towards organising and harmonising external quality assurance schemes in genetic testing. He has also closely collaborated, leading several work groups, with EHDN and International Huntington Association for the review of the predictive guidelines and the development of PGD guidelines for Huntington disease.

He also participated in the OECD expert group that defined the OECD Guidelines for Quality Assurance in Molecular Genetic Testing[9] led the process of defining the EMQN BP Guidelines for the Molecular Genetic Testing in the SCAs (dominant ataxias)[10], and collaborated for the EMQN BP Guidelines for Molecular Genetic Testing of Huntington Disease (still being finalised).

Training and education

There is no formal programme in this area, but some medicine faculties have lectures on rare diseases and information resources (such as Orphanet), and much work is done in high-schools and by patient organisations and health services.

A Professional Master's Course in Genetic Counselling was initiated at the University of Porto. This two-year post-graduation course is an innovative initiative in Portugal for professionals with diverse clinical backgrounds, including clinical psychologists, nurses and others. This full-time programme encompasses bioethics, clinical and genetic epidemiology, genetic counselling principles and techniques, clinical psychology, research methodologies and clinical rotations, as well as one-year training in a recognised medical genetics service and a research project, with special emphasis on rare diseases. The first six genetic counsellors graduated in 2011.

In July 2011, during the post-graduation course "Mental Retardation: from Clinic to Gene and Back" (2nd Edition)[11] a session was about Orphanet services was presented. The audience included molecular and clinical geneticists as well as post-graduation students.

Some patient associations have organised one-day receptions for medical students, so that they are made aware of rare diseases and rare disease patients. Some also organise voluntary rotations for other health professionals, such as social workers and speech therapists.

National rare disease events in 2011

To mark the Rare Disease Day 2011, the Portuguese Alliance of Patients Associations of Rare Disorders (APADR), in collaboration with Orphanet-Portugal, organised a conference on the theme "Rare but Equal", on 26 February 2011. Patients, families, patient associations' representatives, industry representatives, policy makers and health authorities (including the Portuguese Ministry of Health and the Secretary of State for Health, the Vice-Director of Directorate-General of Health, the Social Security Director and the President of INFARMED - the National Authority for Drugs and Health Products), health professionals and researchers and several members of the Scientific Advisory Board of Orphanet-Portugal were present. The Ministry of Health recognised officially the importance of Orphanet activities. Both FEDRA (in Lisbon) and APADR (in Porto) hosted Rare Disease Day events in 2011.

On 11-12 March 2011, the Second Symposium of the *NERD* of the Portuguese Society of Internal Medicine was held in Tomar: the proposed development of a National Registry of Rare Diseases was discussed.

On 10-12 November 2011, the 15th Annual Meeting of the Portuguese Society of Human Genetics was held in Lisbon, with a communication and poster about rare diseases and Orphanet.

Hosted rare disease events in 2011

Amongst the hosted events announced in *OrphaNews Europe* in 2011 were: the 3rd European Phenylketonuria Group Symposium - Advances and challenges in PKU (24-26 March, Lisbon), the Eighth European Cytogenetics

[9] www.oecd.org/dataoecd/43/6/38839788.pdf

[10] www.eurogentest.org/uploads/1283847353000/SCABestPracticeGuidelines-WebsiteVersion.pdf

[11] http://www.icvs.uminho.pt/postgraduation/MentalRetardation/default.aspx

Conference (2-5 July 2011, Porto), the 13th International Conference on Chronic Myeloid Leukemia: Biology and Therapy (September 2011, Estoril), and the European Congress on Myocardial and Pericardial Diseases (13-15 October 2011, Lisbon).

Research activities and E-Rare partnership

National research activities

The public funding agency, Foundation for Science and Technology (FCT), runs several programmes to fund research on rare diseases, as well as the Ministry of Health itself and the private sector.

Participation in European research projects

Portugal participates, or has participated, in European rare disease research projects including: CLINIGENE, EPOKS, Euro-WILSON, SPATAX, EURAMY, EUROCARE CF, EuroGentest-2, EVI-GENORET, LEISHMED, MMR-RELATED CANCER, NEUPROCF, PEROXISOMES, POLYALA, RHORCOD, SAFE, PHGEN, RIBERMOV and SIOPEN-R-NET

E-Rare

Portugal is represented by *FCT* and the Directorate-General of Health, joined the E-Rare project in 2009, for the 2nd Joint Transnational Call: Portugal is represented by a team in one of the projects/consortia selected for funding, with a funding of around €200,000. Portugal did not join the 3rd Joint Transnational Call in 2011.

IRDiRC

Portuguese funding agencies are not currently committed members of the IRDiRC.

Orphan medicinal products

In Portugal, regulation of orphan medicinal products is the responsibility of *INFARMED*. A partnership has been established in 2010 between *INFARMED* and Orphanet for a monthly update on all the orphan medicinal products approved and available in the country.

Orphan medicinal product committee

There is no such committee in Portugal

Orphan medicinal product incentives

No specific incentives are currently in place.

Orphan medicinal product market availability situation

A list of orphan medicinal products launched on the market in Portugal[12] is published on the Orphanet Portugal entry site to the Orphanet database. This data is provided by INFARMED and is regularly updated.

Orphan medicinal product pricing policy

Orphan medicinal product pricing policy fall sunder the responsibility of the Ministry of Health.

Orphan medicinal product reimbursement policy

All Portuguese citizens are covered by the National Health Service, although they may have to participate towards the payment of prescription drugs. There are special programmes in place to facilitate access to growth hormone therapy and enzymatic therapy.

The investment of the NHS in orphan medicinal products in 2011 exceeded €83 million, which represents 8.2% of the total consumption of medicines in hospitals. It should be noted that there was an increase of 15.4% in this group of drugs, as compared to 2010. It must be kept in mind that the total increase in hospital spending in 2011 grew only 1.3%, compared to 2010, when including orphan medicinal products. It must be noted also that 5 orphan medicinal products account for 60% of expenditures in this group (Imatinib, Bosentan, Galsulfase, Lenalidomide, dastinib)[13]. Regardless of its condition of use and supply in Portugal, and

[12] http://www.orpha.net/national/PT-PT/index/lista-de-medicamentos-órfãos-disponíveis-em-portugal/

[13] Source: Consumo de Medicamentos em Meio Hospitalar - Dezembro 2011 http://www.infarmed.pt/portal/page/portal/INFARMED/MONITORIZACAO_DO_MERCADO/OBSERVATORIO/ANALISE_MENSAL_MERCADO/ANALISE_MERCADO_MEDICAMENTOS_CHNM/2011

the status of its current assessment prior to use, all patients within the existing criteria and procedures (e.g. SUA) will have access to therapy.

Other initiatives to improve access to orphan medicinal products

A Special Use Authorisation (SUA) procedure is in place to provide access to certain orphan medicinal products (see section on "Orphan medicinal product availability"). If an authorised orphan medicinal product is not commercialised in Portugal, but marked in other Member States, the treating hospital can request special authorisation from INFARMED: if use is approved, the hospital is directly supplied by the manufacturer, and there is no co-payment from the patient[14].

Orphan devices

Orphan devices also fall under the responsibility of INFARMED.

Specialised social services

Respite care services exist, both in the public, private and social sector, and patients must pay for some services. Other respite facilities are run by patient organisations and some projects have been established with public support. Raríssimas is building a care centre for patients with rare diseases, the construction of which started in July 2010.

Raríssimas has two multidisciplinary centres, which will provide clinical care and therapies to patients and families with rare diseases. There are some therapeutic recreational initiatives organised by hospitals with the support of public or private organisations, which are paid through public and private funding; many programmes are organised by several patient organisations, such as the Portuguese Association for Paramyloidosis. There are some projects to help the integration of patients in daily life, and this offer will hopefully improve under the National Plan for Rare Diseases.

DEVELOPMENT OF RARE DISEASE ACTIVITIES IN 2011 IN PORTUGAL

National plan/strategy for rare diseases and related actions

In November 12, 2008 the Portuguese Minister of Health approved the National Plan for Rare Diseases (*"Programa Nacional para as Doenças Raras"*). A specific tool is already foreseen for the identification of people with rare diseases, aiming at disclosing clinical information to medical doctors and in emergency situations.

The Directorate General of Health, together with the Office of the High Commissioner for Health, have co-funded, in a total amount of €1.9 million, during the years of 2008 to 2011, a few projects on rare diseases, which are currently being developed by several patient associations, what enabled the implementation of a number of strategies mentioned in the National Plan.

Registries

In 2011 the Portuguese Registry of Paramyloidosis was officially established by Order nº 8812/2011 dated 2 June 2011.

National alliances of patient organisations and patient representation

In 2011, FEDRA organised a Conference on "Patients, research and health policies". FEDRA also launched in 2011 the third volume of the publication "Rare Diseases from A to Z", with the collaboration of 36 experts who have reported on around 41 rare diseases, and prefaced by the Director General of Health.

[14] *EMINET Initial investigation to assess the feasibility of a coordinated system to access orphan medicines,* C. Habl, F. Bachner (2011), p57

Sources of information on rare diseases and national help lines

Orphanet activity in Portugal

The Orphanet-Portugal team also created and maintains the Orphanet national entry point for Portugal.

An official event, with media coverage, was held on 26 February 2011 to announce the launch of the Orphanet website in Portuguese, as well as the constitution of the new Scientific Advisory Board. This took place during the conference "Rare but Equal" (*"Raros mas Iguais"*), organised by the APADR in collaboration and with the support of Orphanet-PT, with the presence of the Minister and Secretary of Health, the President of INFARMED (National Authority of Medicines and Health Products), and other health authorities.

In 2011, the Orphanet Portugal team created a Facebook page called "The Orphanet in portuguese" (*"A Orphanet em português"*), hoping that it will become a forum for discussion among all Portuguese-speaking professionals, patients and their organisations, and that it will serve to promote Orphanet in their respective countries. It has already proved useful in helping finding expert volunteers for translations/validations of disease abstracts. In addition, the national team manages a considerable number of questions and inquiries, sent by users mostly by email, requesting information or help.

Other sources of information on rare diseases

The APPDH – Portuguese Association of Parents and Patients with haemoglobinopathies "*APPDH - Associação Portuguesa de Pais e Doentes com Hemoglobinopatias*"), member of *APADR*, published 3 mini-books about haemoglobinopathies, mainly for children, but also useful for adults.

The APN – Portuguese Association of Neuromuscular Diseases (*"Associação Portuguesa de Doenças Neuromusculares"*) a member of APADR as well, published, in 2011, 2 booklets: "Neuromuscular Diseases Manual: for healthcare professionals" ("*Manual sobre Doenças Neuromusculares: Técnicos e Profissionais de Saúde*") and "Neuromuscular Diseases Manual: for patients and caregivers" ("*Manual sobre Doenças Neuromusculares em Idade Pediátrica: Doentes e Cuidadores"*).

Training and education

In July 2011, during the post-graduation course "Mental Retardation: from Clinic to Gene and Back" (2nd Edition)[15] a session was about Orphanet services was presented. The audience included molecular and clinical geneticists as well as post-graduation students.

Some patient associations have organised one-day receptions for medical students, so that they are made aware of rare diseases and rare disease patients. Some also organise voluntary rotations for other health professionals, such as social workers and speech therapists.

National rare disease events in 2011

To mark the Rare Disease Day 2011, the Portuguese Alliance of Patients Associations of Rare Disorders (APADR), in collaboration with Orphanet-Portugal, organised a conference on the theme "Rare but Equal", on 26 February 2011. Patients, families, patient associations' representatives, industry representatives, policy makers and health authorities (including the Portuguese Ministry of Health and the Secretary of State for Health, the Vice-Director of Directorate-General of Health, the Social Security Director and the President of INFARMED - the National Authority for Drugs and Health Products), health professionals and researchers and several members of the Scientific Advisory Board of Orphanet-Portugal were present. The Ministry of Health recognised officially the importance of Orphanet activities. Both FEDRA (in Lisbon) and APADR (in Porto) hosted Rare Disease Day events in 2011.

On 11-12 March 2011, the Second Symposium of the *NERD* of the Portuguese Society of Internal Medicine was held in Tomar: the proposed development of a National Registry of Rare Diseases was discussed.

On 10-12 November 2011, the 15th Annual Meeting of the Portuguese Society of Human Genetics was held in Lisbon, with a communication and poster about rare diseases and Orphanet.

Research activities and E-Rare partnership

E-Rare

Portugal did not join the 3rd Joint Transnational Call in 2011.

IRDiRC

Portuguese funding agencies are not currently committed members of the IRDiRC.

[15] http://www.icvs.uminho.pt/postgraduation/MentalRetardation/default.aspx

LIST OF CONTRIBUTIONS[16]

Contributions in 2010
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- FEDRA - Portuguese Rare Disease Alliance http://www.fedra.pt/
- Alianca Portuguesa de Associaçoes das Doenças Raras http://aliancadoencasraras.org
- Rarìssimas http://www.rarissimas.pt/ and www.linharara.pt

[16] The contributors and validators of the report have contributed information which is accurate to the best of their knowledge. However, readers should take note that the contents of this report are illustrative and not exhaustive.
[17] All websites and documents were last accessed in May 2012. A more detailed list of sources is available in the full report: http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArtRDActivities.pdf