

## State of the Art of Rare Diseases – Activities in EU Member States and Other European Countries

### Romania Report

#### Definition of a Rare Disease

In Romania, stakeholders accept the EU definition of a rare disease laid down in Regulation EC no. 141/2000 on Orphan Medicinal Products, the 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. According to the EU definition a rare disease is defined as a life-threatening or chronically debilitating condition that afflicts fewer than 5 in 10,000 persons within the general public.

#### National Plan

##### Adoption

By the end of 2013 the Ministry of Health adopted the National Plan for Rare Diseases and included it within the National Public Health Strategy for 2014-2020 (“Prosperity of Health”). The National Public Health Strategy and Action Plan for implementing it were approved by Government Decision no. 1028/2014. The strategy established a regulatory, political framework which generates a system to integrate health and social services. Even though the implementation of the integrated care strategy in practice was slowed down by the lack of national legislation and the parallelism of two distinct systems, for health care and social care respectively, responsibilities and budgets being divided between ministries, the Ministry of Health and Ministry of Labour, Family and Social Protection.

A dedicated budget does not exist for the National Plan in Romania. The Government approved, by Decision, the national programmes for rare diseases to be carried out and funded in 2015 and 2016: Ministry of Health (dietary treatment of RDs) and National Health Insurance House (curative treatment for rare diseases).

The funding allocated to the activities of the National Plan was:

- €1,009.193.00 per year which equates to €53,115.421 per million inhabitants.

ICD10 is used for the coding of activities within the Romanian Healthcare system. Orphacode is used as well within local applications (especially Genetic Centres).

There is a dedicated body in place to oversee the drafting or implementation of the National Plan. At the end of 2013 the National Committee for Rare Diseases (NCRD) was created by a Public Health Ministry Order (1215/2013) as an interdisciplinary scientific body without legal personality. The Committee is composed of a total of 20 members including a president, vice president, and a secretary. The NCRD is comprised of healthcare professionals (3), academics (11), representatives of the Ministry of Health (2), National Health Insurance House (1), National Agency for Medicines and Medical Devices (1) and patient representatives (2) as well.

This body plays an advisory role by:

- Providing technical expertise through both its own team and other teams specialised in different areas.
- Developing criteria for the designation of Centres of Expertise for rare diseases
- Drafting the evaluation process and recommending, after the evaluation, the centres of expertise
- Communicating with RONARD (the Romanian National Alliance for RDs) and other institutional partners in order to define together the priorities and to ensure continuity in the patient’s care (information, diagnosis, treatment or specific therapies, counselling, patients and families education, specialists training and their integration into the community).

As a result of continuous activity and effort provided by health planners, policy makers and stakeholders focussed on improving the health, political and legal frameworks, the Ministry of Health issued the order of Centres of Expertise for rare disease (540/2016). Romania has just qualified as a country having a national

strategy for responding to rare diseases and a health political framework in the field. Likewise, it started to implement a few issues of its national plan such as the national evaluation of Centres of Expertise.

### **Organisation of RD Health and Social Care**

#### **Centres of Expertise**

There is a national policy in place in Romania for the designation of Centres of Expertise for rare disease. Ministerial Order 540/2016, an official political decision, developed the framework for the designation of Centres of Expertise for Rare Diseases. Romania uses the EUCERD Recommendation on Quality Criteria for Centres of Expertise adapted to the national level and situation for the designation of Centres of Expertise. The CEs are established to deliver holistic packages of care. The services are designed and commissioned around the needs of rare disease patients. There will be full integration of services with a seamless transition of care between primary, secondary and tertiary healthcare settings, and close partnership working between healthcare, education and social services.

The process of designation is completed for only 9 Romanian healthcare providers.

In Romania there are other dedicated centres around the medical universities and the National Institutes of Health. Even if they are not exclusively dedicated to RD issues they are functioning within a legal framework. In other words, they legally deal with rare diseases but are not officially labelled as Centres of Expertise for rare diseases.

#### **European Reference Networks (ERNs)**

The designation of CEs is the main step towards an application for ERN membership. Romania has in place a formal process for the endorsement of Health Care Providers (CEs) to participate as members or coordinators of an ERN. At present 6 HCPs participate as full members of 6 ERNs in Romania.

<b>Members</b>	<b>European Reference Networks (ERNs)</b>
Clinical Psychiatric Hospital "Alexandru Obregia"	ERN EpiCARE Endo-ERN
Colentina Clinical Hospital	ERN Skin
County Emergency Clinical Hospital	ERN ReCONNECT
Emergency Institute for Cardiovascular Disease "Prof. dr. C. C. Iliescu"	ERN GUARD-HEART
Institute of Oncology "Prof. Dr. Ion Chiricută" Cluj Napoca	Endo-ERN
RoNetwork Multiple Congenital Abnormalities with ID	ERN ITHACA

#### **Rare Disease Registration**

Neither national nor regional rare disease registries exist within Romania but disease specific registries are available. There are no laws or regulations in place governing rare disease registration as yet. The National Committee for RDs deals with the issues of a national registry for rare disease but no public financial resources, so far, have been allocated. Currently NCRD selects the common data elements for rare disease databases and extends the work by ensuring that the dataset are defined in the same way, using the same standards and terms. Also, NCRD is considering appropriate EU standardised databases are in order to find a way to harmonise, share and exchange information. In addition, NCRD has established a baseline measure for data safety and protection. National registries and databases can be used to plan and manage services within the rare disease field.

The registries which are currently in place are managed by academia, clinicians or patient organisations. These include the Romanian biliary atresia registry and Romanian cystic fibrosis patient registry both of which have national coverage. There are more patient registries in the field of rare diseases but the data quality, coverage, governance, and funding support of patient registries are different (the National Registry of Haemophilia, the

National Registry of Hereditary Angioedema, the National Registry of Primary Immunodeficiency, the National Registry of Infant Diabetes Mellitus, the National Registry of Thalassemia, the National Registry for Pulmonary Hypertension, the National Registry for Hyperparathyroidism, the National Registry for Acromegaly, and the National Registry of Neuromuscular Disorders; National Registry of Congenital Hypothyroidism and National Registry of Neuroendocrine Tumours are still under development). Romanian Prader Willi Association has an electronic registry for patients who have benefited from NoRo services since 2015.

Romania contributes to the following European registries: EBAR (European Biliary Atresia Registry), EUROCARE CF (European Cystic Fibrosis Registry) and EUTOS (European Treatment and Outcome Study for Chronic Myeloid Leukaemia).

### **Genetic Testing and Neonatal Screening**

#### **Genetic Testing**

Genetic testing services in Romania are commissioned and delivered in line with current national policy. Genetic testing is voluntary and by law written informed consent must be obtained prior to a person having any form of genetic testing. Testing is available through public or private Medical Genetic Clinics and laboratories. All medical laboratories in Romania need to be accredited to the standards of ISO 15189: Medical Laboratories. Since more than 80% of rare diseases have a genetic basis, six national genetic centres (established by Ministerial Order no. 1358/2014) offer different types of genetic tests:

- New-born screening
- Diagnostic testing
- Carrier testing
- Prenatal testing (invasive and non-invasive tests)
- Predictive and presymptomatic testing
- Forensic testing

Patients are referred for GT by a physician (obstetrician, paediatrician, medical geneticist, haematologist, endocrinologist, and oncologist) but only physicians specialised in Medical genetics are allowed to provide pre- and postnatal testing, counselling and therapy for genetic diseases.

Genetic tests are performed on biological samples: blood, skin, and amniotic fluid or other tissue. The sample is sent to a Genetic Lab in Romania or abroad (if the test is not available in Romania). GT services include cytogenetic and molecular analysis, such as conventional karyotype and interphase and metaphase FISH techniques, and DNA tests (MLPA, QF-PCR, arrayCGH, NGS). The protocols for GT are usually drafted after best practice international guidelines and EU recommendations. Romanian Society of Medical Genetics, academic organizations and NGOs are working to establish the national guidelines for GT based on their own experience as well as national and international documents.

The health insurance does not cover the costs for all genetic tests. Some genetic tests are free of charge (budget allocated for tests is limited) for children and adults who are enrolled in national health programme for birth defects. Other times, the patients could be enrolled in research programmes or non-profit humanitarian programmes so that genetic tests are available free of charge.

Romania included provision for CBGT within its National Plan for rare diseases. A number of specific genetic tests, which as yet are unavailable in Romania, are available abroad. RD patients are able to use form S2 for Health Care Abroad / E112. National Health insurance cards are compulsory but do not work when the RD patient is in another EU country. Romanians are entitled to get a European Health Insurance Card (EHIC) based on which they will receive necessary medical assistance in certain state clinics and hospitals in the public system of the country in question. Not all GT is covered by this card and the beneficiary of medical services may also have to cover some of their medical expenses.

## Neonatal Screening

According to the national health policy a mandatory neonatal screening programme is available for two conditions, phenylketonuria (PKU) and congenital hypothyroidism (CHT), with the goal of screening all newborn babies in Romania. The screening is performed by 4 public medical centres throughout the country (Bucharest, Iasi, Cluj-Napoca and Timisoara) and uses a blood spot test. The current health policy improved the management of screening for PKU and CHT at the local level, reaching 80% coverage for new-borns.

In the last few years, efforts were made through the Health Programme at local level to generalise and improve the organisation of neonatal screening of these two conditions. Neonatal screening tests for other conditions are provided by private clinics / laboratories on demand, at full cost or can be carried out in the framework of research programmes (e.g., hearing loss, metabolic disorders). The Ministry of Health aims to use EU funds to introduce neonatal screening for other rare diseases for which some form of treatment is available (for example, universal new-born hearing screening was approved by MoH at the end of 2016).

## Guidelines and Training Activities

### Clinical Practice Guidelines (CPGs)

There are currently no CPGs for rare diseases at the national level in Romania. Professional organisations, academic organisations and patient organisations are still working to complete this task. There is however national policy in place for the development, adoption and implementation of CPGs in Romania.

### Training and Education

In Romania, there was strong agreement that training and education are a core element of the sustainability of the healthcare system, it should be ensured that sufficient health professionals are trained, with the necessary knowledge and skills. Higher education institutes, such as, Universities of Medicine and Pharmacy are involved in the planning of training and education. They develop curricula designed to meet relevant RD topics ensuring they form part of basic medical training for the undergraduate students. In addition, rare disease is included in optional/ facultative lectures for medical students, as well as postgraduate lectures on Medical/ Clinical Genetics which are organised within major university centres.

The Romanian Society of Medical Genetics provided continuing education for medical doctors and other health professionals, organising training courses every year from 2007 until now.

The Romanian Prader Willi Association ([www.edubolirare.ro](http://www.edubolirare.ro)) has developed a platform for rare diseases, and the training courses are adapted to the needs of different professional working in the field of rare diseases. The training courses are authorised and accredited by the Ministry of Education and Ministry of Work but, also, by National Physicians' Collegium when the training is addressed to medical doctors.

RD training courses for medical journalists, parents and personal assistants were organised in the NORO Centre for RD.

During the last two years other training courses have been provided through RD workshops and conferences organised nationwide.

RPWA has the website ([www.edubolirare.ro](http://www.edubolirare.ro)), an online platform for information and accredited training courses (face to face and online) for different professionals involved in the management of rare diseases.

RONARD has established ([www.aspac.ro](http://www.aspac.ro)), an online platform for training and empowerment of patient organizations and organizational development. Also, RONARD created a website, ([www.participrare.ro](http://www.participrare.ro)), in order to facilitate the involvement, collaboration and communication among all interested parties in the field of rare diseases.

Another educational tool initiated by RONARD is ([www.radionoro.ro](http://www.radionoro.ro)), an online local radio for information about rare diseases at community level.

## **Information Resources for Rare Diseases**

### **Orphanet Activities**

Romania has an operational National Orphanet team who is housed within the University of Medicine and Pharmacy “Grigore T Popa” in Iasi. Due to a lack of funds, technical difficulties and a limited staff there is very little information produced by the Orphanet team. There is no dedicated funding within Romania’s national plan for rare diseases however the Orphanet team has been able to achieve much since the beginning of 2014:

- Advertising Orphanet within different academic, professional and rare disease meetings
- Updating information concerning Romanian services (clinical settings, laboratories) that provide diagnosis and genetic counselling in the field of rare diseases;
- Provide accurate information to persons asking for help and to direct them to the most appropriate service for their needs;
- Represent the interest of the rare disease community within the National Committee for rare diseases (NCRD) (1 Orphanet representative out of 20 members).

### **National Helplines**

There is a helpline in place dedicated to rare diseases in Romania. It is privately funded and is available to both patients and professional individuals. HelpLine is operated by the Romanian Prader Willi Association (RPWA) and it is part of EURORDIS’ Network of Helplines. In the first 2 years of its existence the helpline was funded by the Ministry of Labour but then no more funds were allocated and the helpline is now running through RPWA support. The helpline is coordinated by one person and who stays in contact with a team of volunteers (mainly Doctors/geneticists) all over the country.

### **Official Information Centres**

There are official and unofficial information centres for rare disease within Romania. Romanian Prader Willi Association (RPWA) has established the Information Centre for Rare Genetic Diseases and it is part of NoRo Centre services. It consists of NoRo Helpline and [www.edubolirare.ro](http://www.edubolirare.ro), [www.edubolirare.ro](http://www.edubolirare.ro) and 2 magazines, 1 for patients and 1 for professionals (Rare people and rare diseases and Romanian Journal for rare diseases). With the support of professionals have been published several guidelines for patients, families and professionals for Integrated care in Rare Diseases have been published, patient pathways and a map for care services available at national level, both printed and online: <http://www.participrare.ro/retea-1>.

More information are available on the websites of patient organizations and on the [www.edubolirare.ro](http://www.edubolirare.ro), an online platform for RD information and training.

## **Rare Disease Research Activities**

### **Existence of Rare Disease research programmes/projects**

There are no specific programmes in place to fund or facilitate rare disease research. The national rare disease research comes from the general research budget programmes. The type of research conducted includes basic, clinical and social issues of rare diseases.

### **Participation in E-Rare and International Research Initiatives**

At present Romania participates in neither E-rare no IRDiRC.

### **National Alliance of Patient Organisations and Patient Representation**

The Romanian National Alliance for RDs (RONARD) was established in August 2007 and is a strong voice for a number of patient groups. The Ministry of Health and RONARD work together to define priorities and ensure the continuity of patient care. They provide information, diagnosis, treatment or specific therapies, counselling, patient and family education, specialist training and integration within the community. Currently persons with RDs are consulted and actively encouraged to participate in the design, implementation and

monitoring of health programmes. They participate within the composition of relevant committees and public councils acting in various decision-making processes. As well as RONARD, the national umbrella group, Romania has an additional 120 condition-specific patient organisations, which are all non-profit advocacy groups. They provide information and resources on specific medical conditions, but their activities and resources are also focused on helping the rare disease community and legislation as a whole.

### **Integration of Rare Diseases to Social Policies and Services**

Specific programmes and facilities exist in Romania to support people living with a rare disease. Several laws were put in place to ensure those living with a rare disease are protected. These included:

- The Law of Social Assistance (Law 292/2006- rare diseases with disabilities)
- The Law for the protection and promotion of people with disabilities (Law 448/2011)
- The Law for the insurance of quality in Social Services (Law 197/2012)
- RONARD has established the partnership agreement (nr. 4357/27.04.2016) with the National Authority for Disabled People.

To ensure the multidisciplinary, holistic and continuous provision of care an Interministerial working group for rare diseases was formed which includes representatives from the department of social affairs/services Ministry or equivalent. RONARD has implemented the ColaboRARE Project and created a multidisciplinary/inter-sectorial committee for Rare Diseases and to date has organised four meetings and one national conference, which took place in Bucharest in January 2016.

The Romanian Prader Willi Association (RPWA) is a partner in the INNOVCare project (Innovative Patient-Centred Approach for Social Care Provision to Complex Conditions), which addresses the social challenges faced by people living with rare complex conditions and highlights the gaps in the coordination between medical, social and support services within the EU and its Member States.

INNOVCare is an inter-sectorial and international collaboration, which aims to:

- Innovative care pathway bringing together national resource centres for rare diseases and regional case managers, in partnership with public bodies
- Evaluate the socio-economic impact and a cost-benefit analysis of the care model;
- Exchange good practices & initiate a European network of services;

The Romanian Prader Willi Association, with funding from Norway Grants, was able to create and open the NORO centre in June 2011. Partnered with the Frambu Centre, NORO is a resource centre for rare diseases in Romania. The Centre is recognised as an HCP/Centre of Expertise and participates within a European Reference Network. It forms part of a national consortium, is a one-stop-shop style of service, which is specifically designed for people living with a rare disease. It combines medical, social and educational services creating a bridge between patients/families and various professionals and services involved in patient care. It also ensures that patients are involved at the local, county and national level in all of its services. To ensure a continuous provision of care the NoRo Centre has adopted an individual approach, which ensures patients have an individual care plan.

There are specific measures in place to support the integration of Rare Disease specificities into the national system responsible for assessing a person's level of disability however these measures are still under public debate. In the future, the Ministry of Labour, Family and Social Protection plans to make legislative changes concerning the type and degree of an individual's disability associated with rare disease. At the present, the process is still ongoing.

### **Orphan Medicinal Products**

The list of OMPs available/commercialised in Romania and free of charge through the National Health Programme is available on the website of the Romanian National Agency for Medicines and Medical Devices and includes more than 60 OMPs. In 2017, OMPs for Gaucher disease, Immune Thrombocytopenia Purpura, Duchenne Muscular Dystrophy and Hereditary Angioedema were included in the national list of OMPs.



Romania created a legal framework for compassionate use programmes (Order No 962/2006 on approval of the application of art. 699, paragraph (1) of Law No 95/2006 and Order No 861/2014 on approval of criteria and methodology for assessment of health technologies, of documentation to be submitted by applicants, methodological means used in the assessment for inclusion, extension of indications, non-inclusion into or exclusion from the List of International Non-proprietary Names of on-prescription medicinal products as provided to insurers, irrespective of personal contribution, in the frame of the health insurance system, as well as of International Non-proprietary Names of medicinal products provided in national health insurance programs, as well as the means for appeal thereof. The patients with a severe disease who have no other satisfactory treatment available to them can obtain the medicines through a compassionate use programme.

### **Rare Disease Day**

In Romania, Rare Disease Day has been celebrated since 2007. Romanian people living with or affected by a rare disease, patient organisations, politicians, health professionals, carers, researchers and industry come together in solidarity to raise awareness of rare diseases each year.

Romania, just as any country, used a specific year-by-year slogan:

- The Rare Disease Day 2014 theme "Care" and slogan "Join Together for Better Care"
- The Rare Disease Day 2015 theme "Living with a rare disease" and slogan "Day-by-day, hand-in-hand".
- The Rare Disease Day 2016 theme "Patient Voice" and slogan "Join us in making the voice of rare diseases heard"
- The Rare Disease Day 2017 theme "With research, possibilities are limitless".

Several events and conferences have been organized by the Romanian National Alliance and Romanian Prader Willi Association:

- Europlan workshops in 2014, 2015, 2016 with the participation of the Europlan coordination team,
- National workshop in 2015 and National conference in April 2016 on integrated care in the context of NoRo- Frambu,
- The partnership for the future project,
- A National conference called ColaboRARE on 29-30 January 2016 and the Expert Rare Conference - dedicated to Centres of Expertise for Rare Diseases on 14-15 July 2016.

On June 30, 2016, RONARD organized, in partnership with EURORDIS, a workshop dedicated entitled "The Improvement of access to treatment and therapies for people living with rare diseases in Romania".

### **Other**

Between 2014 and 2017, all the Romanian stakeholders, including patients, health professionals, policymakers and academia worked together and made some notable progress towards improving the quality of life for RD patients. But more is needed.

On a national level, Romania has:

- Gained the recognition and acceptance of rare diseases as a priority for health care in Romania;
- Expanded the official Political Decision that support the designation of CEs for RDs, using the EUCERD Recommendations on Quality Criteria
- Ensured Centres of Expertise have adapted to the national situation, and the application for ERN membership.