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

Croatia Report

Definition of a Rare Disease

Croatia has adopted the European Commission definition of a rare disease (i.e. no more than 5 per 10,000 people, as per *Regulation* (EC) No 141/*2000*). The National Plan espouses this definition.

Status Quo of any National Plan or Strategy for Rare Diseases

The National Programme for Rare Diseases 2015-2020 was adopted by the Croatian government on 5 March 2015. There is a modest funding budget for the activities of the National Plan. Most of the budget is dedicated to cover the cost of patient treatment. Each activity of the National Plan is costed but at present only a small amount is allocated to the activities of patient organisations.

There is a dedicated body in place to oversee the drafting and now implementation of the National Plan. The committee is multistakeholder and meets regularly. Membership of the committee is as follows:

- Professionals (1 medical geneticist, 1 paediatrician, 1 metabolic disease expert, 1 paediatric oncologist, 1 haematologist)
- 1 representative of Croatian Medicine Agency,
- 2 representatives of the Croatian Institute of Public Health
- 1 representative of Patient Organisations
- 1 representative of the Croatian Health Insurance Fund
- 1 representative of the Ministry of Social Affaires

In 2016, meetings were held every three months to address the activities, timeline etc. of the National Plan. A Report of the meetings of 2015 is currently being prepared.

The National Plan has resulted in several positive outcomes. In 2015:

a) Centres of Expertise were identified for rare diseases: nine were formally appointed by the Ministry of Health.
b) The Croatian Institute of Public Health began to collect data for the RD Registry. The Croatian Society for Rare Disease of the Croatian Medical Association funded the creation of software for the Registry on rare diseases.
c) Orphanet Croatia became operational

In 2016 progress has continued, and highlights include the following:

a) Appointment of the hospital coordinators for rare disease patients (in each major hospital in Croatia)
b) Translation of the National Plan into English
c) The organisation of the 4th Symposium on Rare Diseases and the 4th National Conference on Rare Diseases which took place on 12 February 2016, under the auspices of the President of the Republic of Croatia.

Amongst other priorities, the National Plan is considering the possibility of introducing OrphaCode in the health information system in addition to ICD 10.

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Organisation of Rare Disease Health and Social Care (Centres of Expertise; ERNs; Integrated Care and Social Support)

Centres of Expertise (CEs)

Croatia has an official policy for the designation of Centres of Expertise (here *Excellence*) for rare diseases. This formal, national policy has now been fully implemented and will be evaluated every 5 years.
The national criteria, used to designate CEs, were created before the EUCERD criteria. The criteria are not specific to the Centres of Excellence for *rare disease*, but for all Centres of Excellence in Croatia. The requisite criteria include:

- Proof of scientific and professional results in the follow-up, study and improvement of diagnostics and treatment for a particular condition/ set of conditions for a period of at least 5 years;
- Collaboration with prominent institutions of the same field, manifested through the exchange of experts, joint research projects and other forms of cooperation;
- The Centre of Excellence should demonstrate continuous success in scientific projects, application of new diagnostic or therapeutic methods and procedures, and should secure an adequate number of qualified staff, superior equipment and adequate facilities.

To some extent, CEs ensure a holistic approach to care; however, there is more to be done in this area.

European Reference Networks (ERNs)

At present 1 Health care provider (HCP) is participating as a full member in 2 ERNs (https://ec.europa.eu/health/ern_en):

Member	European Reference Network (ERN)
University Hospital Zagreb	MetabERN ERN Skin

Integration of Rare Diseases to social policies and services

Programmes/facilities exist in general for patients with disabilities (although are not specifically tailored for people with rare diseases *per se*). Individual care plans are available, which include details of access to social and support services. At present, these care plans are only organised at the levels of Centres of Excellence.
In terms of measures to support the integration of rare disease specificities into the national system responsible for assessing a person's level of functioning: when a patient with a rare disease is evaluated, an expert opinion from outside of the appointed Committee is required.

Croatia has several planned activities to support the social integration of people with rare diseases. These include:

1. The organisation of an information system for people affected by rare diseases which provides guidance on how they can exercise their rights in the social welfare system.
2. The development of support services in the local community
3. The organisation of respite care centres
4. The inclusion of rare disease experts to the list of experts who evaluate a patient's level of disability/functioning
5. Ensuring participation in the training of experts/members of the first evaluation body and employees of social welfare centres

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6. Ensuring the active participation of patient organizations in the formation of regulations and laws regarding persons with disabilities.

Rare Disease Registration

No national or regional-level registries exist for rare diseases in Croatia.

Genetic Testing and Neonatal Screening

Genetic testing is organised mostly in major clinical hospitals (and to a lesser extent, in scientific institutes). The Croatian Institute for Health Insurance covers genetic testing abroad if the test is not available in Croatia and if it is demonstrated that the test is of importance for the management of patient.

At present the Neonatal screening programme in Croatia tests for two conditions: phenylketonuria and hypothyroidism.

Clinical Practice Guidelines and Training Activities

Clinical Practice Guidelines (CPGs)

In Croatia, several guidelines have been published by Rare Disease Experts, for example on Gaucher Disease. There is no national policy for the development or implementation of CPGs but there is a policy in place for the adoption of CPGs for rare disease at the national level.

Training and Education

An educational meeting for regional leaders of patient organisations for rare diseases took place in October 2016 in Split, Croatia. Training on the coding of congenital anomalies will be taking place in December 2016.

Information Resources for Rare Diseases

Orphanet Activities

Croatia has an operational National Orphanet team which is hosted by Rare Diseases Croatia.
To date, only a few documents have been translated into the Croatian national language: they can be found on the dedicated webpage. The National Plan aims to prepare information in Croatian regarding the most common rare diseases, those which have ICD10 codes. This activity should be funded by National Plan budget.

Currently no funding has been specifically dedicated to the activities of the national Orphanet team.

Since 2014 the Orphanet team has created a website and made several presentations on their activities at national conferences (Human Genetics Conference in 2015, Rare Disease Symposium in 2016). They have

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actively engaged with the rare disease community to endorse departments, laboratories and professionals to encourage the entering of data into the Orphanet database.

National Helplines

There is a helpline in place dedicated to rare diseases in Croatia. It is funded through a mixture of public and private funding and is available only to patients. Patient organisations receive questions from users and try to answer them as best they can through consultation with professionals. Patient organisations have also engaged with medical students to help them in answering the questions of patients.

Rare Disease Research Activities

In the National Plan, it is outlined that all research activities related to rare diseases -including those with a social and/or economic focus- should be identified and supported with special funds; however, this has not yet been achieved.
Research is currently funded through different sources and it is difficult to provide an overview of rare disease research in Croatia. This is why the National Plan insists that all RD projects be reported separately.

At present, Croatia participates in neither E-RARE nor IRDiRC.

National Alliance of Patient Organisations and Patient Representation

There is a national alliance of rare disease patient organisations in Croatia. To date the main achievements of the national alliance at the rare disease helpline and Orphanet Croatia. The level of representation and consultation of rare disease patients at the regional or national level has been modest but patients form part of the Committee for the National Plan. Before 2015 there were three patient representatives, a new representative has been recently been appointed by the Ministry of Health.

Orphan Medicinal Products (OMPs)

At present, 100 OMPs are available in Croatia, according to the information here:
http://www.halmed.hr/Lijekovi/Informacije-o-lijekovima/Lijekovi-za-lijecenje-rijetkih-i-teskih-bolesti/

Some measures are in place to facilitate access to OMPs for patients; specifically, Compassionate Use is possible. There are no incentives at present to support research into -and the development of- OMPs ((designated or potential); however, looking forwards, measures to support future research into OMPs/Rare Diseases and to increase the availability of OMPs to patients are both envisaged under the National Plan.

Rare Disease Day

Croatia organises many events to celebrate Rare Disease Day each year. Since 2014, the following events have taken place:

- The National Conference on Rare Diseases, Zagreb, February 12 2016
- The 4th Croatian Symposium on Rare Diseases, Zagreb, February 13 2016
- The 3rd Symposium on Rare Diseases, Zagreb, February 28 2014

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- The 3rd National Conference on Rare Diseases, Zagreb, February 27 2014
- Rare Disease Day manifestations organised by patients' organisations each year include - meeting with the president of Republic of Croatia, the issuing of press releases, round table meetings and participation in radio and TV shows.

In 2015, the following events were organised:

- February 27 2015 - cinema premiere of the documentary "Day after day" on RD patients that was also shown on national TV.
- Presentation of the Patient Alliance for RD in all major cities of Croatia on February 28 each year.
- A campaign entitled "Embrace for Rare Diseases" exhibited photos taken across Croatia of people supporting Rare Disease Day.
- Marking the Day of MPS, Gaucher, Pompe disease, CF week, epidermolysis bullosa week etc.
- The T-portal: the series "You have no idea about them" – presented stories about patients with rare diseases.

Additional Achievements since 2014:

The main areas of improvement relating to rare diseases in Croatia are as follows: a greater level of awareness in the general population regarding the problems faced by those with a rare disease; the funding of patient organisations; and the adoption of the National Plan for rare diseases.

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