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

Belgium Report

Definition of a Rare Disease

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

Status Quo of any National Plan or Strategy for Rare Diseases

The National Plan for Rare Diseases was adopted in December 2013. The Plan is not enshrined in any single law or decree; however, a specific legal framework *has* been created for some of the actions defined in the NP. There is no set time-frame for the NP, which is directly funded by a policy decision, to the amount of €15m per annum.

Context for the adoption of the National Plan:

The Belgian NP for RD emerged partially from an increased recognition of the needs of people with rare diseases, which in turn resulted from the development of the Belgian Cancer Plan and the National Plan for Chronic Illness. In February 2009, the Belgian House of Representatives adopted a resolution for a plan of action for rare diseases and orphan medicinal products. The 'Fund for Rare Diseases and Orphan Drugs', managed by the King Baudouin Foundation, was financially supported for two years (2009-2011) under the framework of the Belgian Plan for Chronic Diseases, to develop a proposition for a Belgian Plan for Rare Diseases. Working groups within this 'Fund for Rare Diseases and Orphan Drugs' developed a set of recommendations which grouped specific measures into different domains. These recommendations were elaborated in two distinct phases: Phase 1 concerned recommendations elaborated in 2010 for the following four central topics: (1) diagnostics and treatment; (2) codification and registration; (3) information, awareness, and patient empowerment; and (4) access and cost. Phase 2 concerned recommendations elaborated in 2011 for the following topics: nonmedical costs of rare diseases; international networking, research, adherence; advanced therapy medicinal products, ethical issues, teaching and education, including therapeutic education and finally, clinical trials.

A Steering Committee appointed by the Minister of Public Health was established, which analysed the proposals in terms of financing and in view of the existing plans for cancer and chronic diseases. At the end 2013, the draft Plan -based on the analysis of this steering committee- was eventually adopted by the Minister of Public Health.

Twenty actions were identified across 4 main categories: each point was accompanied by specific tasks, budgets, and lead authorities. These 4 main categories were as follows:

- improvement of access to diagnostics and information for patients;
- optimisation of healthcare;
- improvement of knowledge generation
- governance and sustainability of the plan.

Implementation and Monitoring of the National Plan

A dedicated body is in place to oversee the implementation of the NP, namely the '**Steering Group for Rare Diseases'**, which is composed of representatives of the following:

- The Minister of Public Health
- National Health & Disability Insurance
- Scientific Institute of Public Health
- Ministry of Health

This body may most accurately be described as 'partially functioning' in the sense that it does not meet regularly and does not yet involve all the relevant stakeholders (for instance patients).

To-date, the National Plan has achieved numerous successes, including the following:

- Formation of a legal framework regarding the organisation of rare diseases
- Development of a quality system for use in the genetic centres
- Development of a central registry for rare diseases, currently receiving data via the genetic centres
- Introduction of OrphaCodes in the genetic centres

The NP addresses the important issue of coding rare disease in health information systems.

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

Centres of Expertise

Belgium has both a national and regional designation process for Centres of Expertise. There are several centres specialised in one rare disease or a group of rare diseases. Some of these centres are recognised by the National Institute for Health and Disability (NIHDI) and work under a convention. Rare diseases covered by these centres include: cystic fibrosis, metabolic diseases and neuromuscular diseases and haemophilia.

In addition, a legal framework for centres of expertise and networks for rare diseases has been established in August 2014. The responsibility for recognition and designation of these centres is a shared federal and regional responsibility. At this time, 7 university hospitals have obtained a recognition from regional health authorities for a 'rare diseases function' based on general criteria in the legal framework. In a later stage, specific centres of expertise can be designated.

The national criteria for the organisation of care for rare diseases are described in the Royal Decree of 25/04/2014. These criteria were inspired by the EUCERD criteria.

European Reference Networks (ERNs)

A formal process was put in place for endorsing Health Care Providers to participate in the application of an ERN. At present, 10 HCPs participate as full members of 23 ERNS in Belgium. (For a full list, see https://ec.europa.eu/health/ern_en)

Integration of Rare Diseases to Social Policies and Services

Programmes and facilities exist to support people with rare diseases. Specific facilities for respite care and therapeutic recreational programmes are under investigation however, but do not currently exist in a structured fashion exclusively for rare diseases.

A budget was allocated for the financing of respite care structures for children with chronic diseases, including rare diseases patients. Three projects were started in 2011. Governmental measures for the integration of handicapped persons already exist in Belgium by means of social and financial support. The NIHDI reimburse for

the transport cost for the children who are in treatment in a Centre of expertise.

Continuous care is planned through resource centres for rare disease - 'one stop shop style' social services for rare diseases. The case managers and resource centers are not yet operational but they are planned and budget has been reserved. Social integration of people with rare diseases is provided for in the system currently devised to support all citizens.

Rare Disease Registration

Belgium has a national registry for all rare diseases, known as the Central Registry for Rare Diseases (CRRD).

- During an initial 'proof-of-concept' phase (lasting from Dec 2013 – Jun 2015), **the CRRD began prospectively collecting a limited set of core variables from two genetic centres.**
- Subsequently, the other six officially-recognized genetic centres began to contribute data also.
- Detailed (technical) information can be found at http://www.healthdata.be/nl and the list of variables collected is available here - http://www.healthdata.be/dcd/#/collection/41#top.
- Around 1000 patients have been registered with the CCRD.
- In terms of codification systems, the CRRD uses the OrphaCode alongside other coding systems (ICD10, ICD-O, OMIM, Snomed, HPO, ISCN, and LOINC).
- Some hospitals are now working on the integration of data from electronic health records (EHRs)

In addition to the CRRD, Belgium has two national-level disease-specific registries:

1. The **Belgian Cystic Fibrosis Registry (BCFR):**
   - Commenced operations in 1998 and is well-established, with an annual data collection of more than 200 variables.
   - As of 2013, 1186 patients have been registered (which is estimated to account for over 90% of the CF population).
   - This registry does not use the OrphaCode (as only one condition is included).
   - More data are available here - https://www.healthstat.be/

2. The **Belgian Registry for Neuromuscular Diseases (BNMDR):**
   - Annual data collection for the (BNMDR) began in 2008.
   - The data is provided by 7 national reference centres for neuromuscular diseases.
   - Since 2015, the data collection tool 'Healthdata.be' has been used (see https://www.healthdata.be/dcd/#/collection/189#top for the list of data items collected)
   - As of 2015, 4760 patients had been registered in this national Neuromuscular Diseases registry.
   - The BNMDR currently uses two classifications: the National Institute of Health and Disability Insurance (NIHDI) classification and a "Belgian" CRAMP classification, adapted from the Dutch CRAMP classification. BNMDR is planning to add the following classification systems: OrphaCode, OMIM, and ICD-10.

These national registries are funded solely by the National Institute of Health and Disability Insurance (NIHDI). The objectives of the Belgian national registries are as follows:

- Epidemiological research
- Quality of care
- Sharing data at EU level
- Facilitation of patient recruitment for trials

Finally, Belgian clinicians contribute to European (e.g. EUROCAT) level and international registries.

Several Laws govern rare disease registration in Belgium:

1) An important law with regard to the registration of health-related personal data is the Privacy Law. Specific authorizations must be obtained from the Privacy Commission for any registration project, and for any *change* in such a project (e.g. changes in the variables collected, in data providers, data flow, etc.). The Privacy Commission publishes its decisions, and the conditions under which authorisations are granted, on its website (www.privacycommission.be). For example, for the Central Registry Rare Diseases see https://www.privacycommission.be/de/documents/19076.

2) Several laws or regulations exist which oblige specific care providers to register the data of rare disease patients (for example, within the context of recognition as a reference centre). In some cases, the data which must be registered and the registry concerned are actually specified; for example, conventions of revalidation between the National Institute of Health and Disability Insurance (NIHDI) and the reference centres specify a requirement for registration via the Belgian Cystic Fibrosis Registry (BCFR) and the Belgian Neuromuscular Diseases Registry (BNMDR). Documents can be found on the website of the NIHDI, www.riziv.fgov.be. The genetic centres also have an obligation to register epidemiological data (http://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?language=nl&la=N&cn=1987121432&table_name=wet)

3) Health-related registries must all conform to the requirements stipulated in the Belgian eHealth Roadmap 2013-2018 (www.plan-egezondheid.be).

Genetic Testing and Neonatal Screening

Genetic Testing:

Genetic testing in Belgium is carried out **exclusively by eight Centres for Human Genetics** – the operational standards for these 8 Centres are established by Royal Decree. All genetic centres have obtained accreditation of their diagnostic activities. Specific reimbursement conditions for genetic tests have been organised in a stratified reimbursement system (activities are reimbursed by the NIHDI): **this includes a comprehensive list of diagnoses and genes for which testing is available in Belgium**. According to the Orphanet database, at the end of 2016, genetic tests were available in Belgium for 547 diseases and 689 genes (excluding panels of genes).

Genetic testing abroad is possible, when referred by the Belgian Centres for Human Genetics: the Centres send the samples to a foreign reference laboratory. Any genetic tests carried out abroad are reimbursed by convention with the 8 Belgian Centres for Human Genetics.

Neonatal Screening:

In Belgium, neonatal screening is the responsibility of the communities: in both the Walloon region and Flanders, neonatal screening is organised by the health authorities of the communities. Screening is regulated in the regional legislation, as follows:

- Flanders: Decree of the Flemish government of 12 December 2008 concerning population screening and Decree of 5 June 2009 concerning recognition and funding of partner organisations. The following diseases are included to the screening programme: Biotinidase deficiency, Glutaric acidemia type 1, Isovaleric acidemia, Leucinosis or Maple syrup urine disease, Medium chain acyl-CoA dehydrogenase deficiency, Methylmalonic acidemia, Multiple acyl-CoA dehydrogenase deficiency, Phenylketonuria, Propionic acidemia, Congenital hypothyroidia, Congenital adrenal hyperplasia **(= 11 diseases)**

- French Community: Decree of French Community government of 29 May 2009 concerning screening for congenital anomalies. The following diseases are included to the screening programme: Galactosemia, Glutaric acidemia type 1, Homocystinuria, Isovaleric acidemia, Leucinosis or Maple syrup urine disease, Medium chain acyl-CoA dehydrogenase deficiency, Methylmalonic acidemia, Multiple acyl-CoA dehydrogenase deficiency, Phenylketonuria, Propionic acidemia, Tyrosinemia Type I, Very long Chain CoA deshydrogenase deficiency, Congenital hypothyroidia **(= 13 diseases).**

Clinical Practice Guidelines and Training Activities

Clinical Practice Guidelines (CPGs)

Belgium has not produced any CPGs on Rare Disease at the national level. There is a national policy in place for development and adoption of Guidelines, but no currently for their implementation.

Training and Education

Training initiatives are included as part of both general education and specific training within each medical discipline.

Information Resources for Rare Diseases

Orphanet Activities

A National Orphanet Team for Belgium is operational and based at the Scientific Institute of Public Health (WIV-ISP). This institution is a partner of RD-Action. Belgian health authorities are financially responsible for participation in RD-Action.

The team fulfills the Orphanet tasks as described in the RD-Action project - registration, annual updates, quality control, et cetera. The team also responds to a high demand for participation in other rare disease related projects.

National Helplines

A mixture of public and private funding supports the national alliance Radiorg in providing a helpline to both patients and medical professionals. The organization also responds to queries online and via post, through a network of volunteers. Radiorg works in collaboration with RDB, a French speaking rare disease association composed mainly of retired geneticists who offer their experience and knowledge to individual patients.

Official Information Centres

There are no official information centres for Rare Disease in Belgium.

Rare Disease Research Activities

There is currently no specific research project or programme into rare disease operating in Belgium. The FRS-FNRS (Fund for Scientific Research, French-speaking community of Belgium) and its associated FRSM (Fund for Scientific Medical Research) provides funding for basic research on rare diseases including rare cancers.

Rare disease research also benefits from initiatives such as programmes to stimulate translational R&D. Some fundraising patient organisations also finance rare disease research.

Currently Belgium is a participant in E-rare. FNRS and FWO participate in e-Rare and a member of a Belgian university participates in the Diagnostic Scientific committee of IRDiRC.

National Alliance of Patient Organisations and Patient Representation

RaDiOrg is the contraction of Rare Diseases Organization Belgium. It forms the Belgian umbrella association for rare disease patient organisations and people suffering from a rare disease. RaDiOrgis recognized as national alliance by EURORDIS, the European Federation of Rare Diseases and member of the CNA (Council of national alliances).

Since 2014, the alliance has specifically achieved:

1. A new communication plan: upgrade of website and newsflash, online calendar for our members and an online forum for questions (helpline).

2. Better support of our member organisations by stimulating them to join Rare Disease Day (small grants for a local awareness campaign) and the Edelweiss award for the best communication campaign.

3. Strategic audit in order to professionalize the alliance

RaDiOrg is represented in various rare disease related bodies, including:

- Fund for Rare Diseases and Orphan Drugs, King Baudouin Foundation
- Observatory for Chronic Diseases including a special workgroup on rare diseases
- A Flemish committee preparing a Flemish network on rare diseases
- A Flemish working group on neonatal screening
- Substitute member of the board of KCE (Belgian Healthcare Knowledge center)
- WIV-ISP: committee central register
- Associate member in cross border project EmRaDi (kick-off October 2016)
- FAGG (medicine agency): patients represented by the Flemish and Walloon platforms VPP and LUSS (not by RaDiOrg))

Orphan Medicinal Products (OMPs)

As of November 2016, 78 Orphan Medicinal Products (OMPs) are available in Belgium, according to the National Institute for Health and Disability Insurance, who have made the information publically available online. The ETA/ETR program is designed to assess unmet medical needs for patients, and facilitate their access to OMPs. Specific approvals are in place for pricing and reimbursement, and there are incentives supporting research and development into OMPs.

Rare Disease Day

RaDiOrg (Rare Diseases Organisation) joined the EURORDIS events in Brussels in 2015 and 2016. . They had an information booth and invited their members to attend the symposium. They also organized a parallel members meeting.
RaDiOrg works together with CANTILIS for all communication aspects.

In 2016 the members were asked to organize an awareness event which would combine awareness for their own disease and at the same time for the rare disease community in general. The Edelweiss award went to the association AKABE (Kabuki) for their great communication package.

Main achievements since 2014:

Ultimately, the main area of improvement has been the introduction of legal framework supporting health care for those with rare diseases.