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

Austria Report

Definition of a Rare Disease

Austria formally 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*) in February 2015, when the National Plan for Rare Diseases was adopted. There are no instances when a different definition is used.

Status Quo of any National Plan or Strategy for Rare Diseases

Elaboration and Adoption:

The Austrian National Plan for Rare Diseases (NAP.se) was developed and written by the National Coordination Centre for Rare Diseases (CCRD), which was established by the Austrian Ministry of Health in April 2011.
Two committees were established to accompany the activities of the CCRD:

- the Expert Committee on Rare Diseases, which includes representatives of a variety of stakeholders in the rare disease field in Austria
- the Strategic Platform, which includes delegates of the decision-makers in the Austrian health care and social system.

These two committees participated actively in the development of the NAP.se. Once the draft was complete, the input of all relevant decision-makers was obtained, and the NAP.se was eventually approved by and published on behalf of the Austrian Ministry of Health as well as the Ministry of Labour, Social Affairs and Consumer Protection, and the Ministry of Science, Research and Economy. The NAP.se is not enshrined in any legislation; however, through the elaboration and approval process outlined above, one can assume a broad acceptance of the plan among rare disease stakeholders in the healthcare, social services and research fields.

There is no dedicated funding associated with the NAP.se itself; however, the budget for the National Coordination Centre for Rare Diseases (CCRD), which is in charge of the *implementation* of the National Plan, is negotiated with the Austrian Ministry of Health and Women's Affairs on an annual basis. Currently, this budget amounts to about 1 full time equivalent. These costs are integrated in the general budget of the Austrian Health Institute, where the CCRD is located and which is funded by the Ministry of Health and Women's Affairs.

As above, a dedicated body oversaw the elaboration and now the implementation of the National Plan: the *Expert Committee on Rare Diseases* was established in 2011 to support the activities of the CCRD, including the **implementation** of the National Plan. This Expert Committee meets regularly and is multistakeholder in composition (including patients). In 2015, the Committee became the official advisory board for rare diseases of the Austrian Ministry of Health and Women's Affairs. The biannual meetings of the Expert Committee are organized by the CCRD. The following stakeholders are included:

- Patient organizations (4 members)
- Austrian Medical Chamber (1)
- Medical Experts (including new-born screening, genetics, paediatrics) (6)
- Ministry of Labour, Social Affairs and Consumer Protection (1)
- Ministry of Science, Research and Economy (1)
- Main Association of Austrian Social Security Institutions (1)
- Vienna Regional Health Insurance Fund (1)
- Representatives of public hospitals (1)
- Representatives of local governments (2)

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- Austrian COMP-member (1)
- Pharmaceutical industry (umbrella organization) (1)
- Medical ethics (1)
- Ministry of Health and Women's Affairs
- CCRD/Orphanet Austria

Content and Achievements of the National Plan

A section of the National Plan is dedicated to the implementation of an adequate coding system for rare diseases, to allow for better epidemiology and reimbursement.

To date, the prominent measures implemented under the National Plan include the following:

- Establishment of the National Coordination Centre for Rare Diseases, CCRD, (2011) including its two accompanying committees (Expert Committee on Rare Diseases and the Strategic Platform). Biannual meeting with each committee
- Development of a designation process for centres of expertise for rare diseases in Austria by the CCRD (two healthcare providers were involved in the pilot process and will be officially designated in December 2016 and March 2017)
- Nationwide mapping of clinical expertise for rare diseases in order to identify further candidates for official designation as a centre of expertise for rare diseases (close collaboration between Orphanet Austria and the CCRD)
- Initiation of the following processes concerning rare disease policy: integration of an adequate coding system for rare diseases in Austrian health information systems; development of a patient information card (or electronic device) for rare disease patients
- Establishment of a work group for laboratory diagnostics of rare diseases; workshop on rare disease epidemiology / patient registries (strategy concerning registries to be developed in context with the strategy for the coding system); various PR-related actions (organization of a EUROPLAN-conference, production of texts on rare diseases for the Austrian health portal, answering of patient/stakeholder requests, presentations at conferences and at stakeholder events, newspaper/journal articles etc.).

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

Centres of Expertise

Austria has adopted a formal National Policy for designating Centres of Expertise: the designation process can be considered 'fully implemented' as of December 2016, as this was the date of designation of the first official Centre.

The National Plan for Rare diseases (NA.se) lists an array of criteria which were adapted from the EUCERD criteria and are very similar in their content. These basic criteria were subsequently transformed into concrete operational criteria listed in an official questionnaire. This catalogue includes general criteria applying to all potential centres, as well as specific criteria, which are to be developed separately for the respective field of expertise. The criteria are closely related to those for individual healthcare providers (HCPs) participating in an ERN.

There are **two Centres of Expertise** which comply with the formal National Policy in Austria. Moreover, there are thirty Centres complying with the *EUCERD* criteria for a CE. In terms of holistic care - patient care in Austrian Centres of Expertise must be provided by a multi-professional team comprising not only all the relevant, necessary medical personnel, but also non-medical personnel like social workers, etc.

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European Reference Networks (ERNs)

A formal process is in place for endorsing HealthCare Providers (HCPs) to participate as members or coordinators of an ERN: at present 1 HCP is participating as a full member in 2 ERNs, and indeed is the Coordinator of the ERN PaedCan (https://ec.europa.eu/health/ern_en):

Member	European Reference Networks (ERNs)
St. Anna Kinderspital & St. Anna Kinderkrebsforschung EB-Haus	ERN PaedCan ERN Skin

Integration of Rare Diseases into Social Policies and Services

There are currently no plans to specifically support the integration of people with rare diseases into daily life.

Rare Disease Registration

Currently, neither national nor regional Rare Disease registries exist, but disease specific registries are available. It is foreseen in the National Plan that designated centres of expertise for rare diseases will be obliged to establish/ continue/ contribute to registries specific for the respective group of rare diseases.

Registries for single rare diseases or groups of rare diseases do exist in Austria and are currently clinician-led. Only larger registries dealing with large groups of both rare and non-rare diseases (like the Austrian Cancer Registry) are in public hands. This means that typically, not all Austrian patients with a specific disease are registered, as the registries are mostly local initiatives, and participation is not mandatory.

Registries presently listed in Orphanet cover the following diseases or groups of diseases: CF; MSA; brain tumours; alpha 1-antitrypsin deficiency; mastocytosis; NHL in children and adolescents; ALL in children and adolescents; aHUS; alternating hemiplegia and rare epilepsies; T-cell lymphomas; inborn errors of metabolism; multiple myeloma; echinococcosis; CML; squamous cell carcinoma of the head and neck; acromegaly; epidermolysis bullosa; myelodysplastic syndromes; GIST; haemophilia; Upshaw-Schulman syndrome; histiocytic disorders; Behcet disease; cancer predisposition syndromes; congenital anomalies; ALL. (Please note that this content is in the process of being updated in the frame of the nationwide mapping process for clinical services for rare diseases.)

Genetic Testing and Newborn Screening

Genetic testing in Austria is regulated by the Gene Technology Act which was first established in 1994 (http://www.bmgf.gv.at/cms/home/attachments/7/8/8/CH1060/CMS1226929588865/510_1994.pdf) This Act covers all legal, ethical and (bio-) safety aspects regarding diagnostics and research in the field of molecular genetics. In the chapter on human molecular genetic testing, genetic tests are subdivided into four types:

- Type 1 comprises tests to identify either concrete somatic changes in the number, structure, or sequence of chromosomes, genes or DNA fragments or concrete chemical modifications in chromosomes, genes or DNA fragments in patients suffering from a symptomatic and diagnosed disease (for instance, the search for a somatic mutation or altered methylation status in a tumour tissue sample).
- Type 2 covers testing for germline mutations in patients suffering from a symptomatic and diagnosed disease.

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- Type 3 comprises tests to establish the genetic risk/predisposition of a healthy individual to potentially develop a genetic disease in the future, or to establish the carrier status of a healthy individual for a certain genetic disease, in disorders where prophylaxis or treatment are available.
- Type 4 covers tests which establish the genetic risk/predisposition of a healthy individual to potentially develop a genetic disease in the future, or establish the carrier status of a healthy individual for a certain genetic disease, in disorders where prophylaxis or treatment do not exist.

While no authorisation is needed for tests within categories 1 and 2, tests within categories 3 and 4 can *only* be performed in laboratories officially authorized by the Austrian Ministry of Health and Women's Affairs. Institutions seeking authorization must register their activity and submit a detailed description of their facilities, equipment, technical procedures, quality schemes, and experience in genetic testing. The formal authorization for the respective genetic test is granted after an evaluation process, which includes consultation of the scientific board of the Committee on Gene Technology. **Laboratories performing genetic testing in Austria are listed in a registry administrated by the Ministry of Health and Women's Affairs**. There are, however, no official reference laboratories in Austria.

Austrian laboratories are actively contacted by the local Orphanet-Team and so provide details upon request. All major genetic laboratories are registered with Orphanet. **At the end of 2016, the Orphanet database recorded that Austrian laboratories were able to test for 703 genes (excluding panels of genes) and 745 rare diseases.**

Reimbursement of genetic testing costs is primarily a responsibility of the individual Austrian states and as a rule is not centrally regulated (there *are* some exceptions). This responsibility is further divided between two different types of institutions, depending on whether the patient had been treated in a hospital (inpatient or outpatient) or in private practice (with a service contract with the relevant health insurance fund). In the first case, the hospital bears the costs of any diagnostic test. The hospital, in turn, is indirectly reimbursed by the health fund of the respective state on a DRG (Diagnosis-Related Group) basis. For private practice, the patient's health insurance covers the costs. Tariffs are calculated by the health insurance agencies and listed in a catalogue, which is updated annually. However, reimbursement is also possible for tests that are not listed in this catalogue upon individual application. In some instances (for example if the costs exceed a certain threshold), testing requires prior authorization by the chief physician of the insurance agency.

Genetic testing abroad is possible as soon as the test is strongly indicated for an individual patient and either a) cannot be performed at all within the country, or b) cannot be performed easily. In these cases, prior authorization by the insurance agency (private practice) or the hospital director is obligatory. Other than that, the general rules described above apply.

Newborn Screening:

Austria's newborn screening program was established in the 1960's by the Ministry of Health and the Ministry of Science and Research. The service is located at the Department of Paediatrics and Adolescent Medicine of the Medical University of Vienna. Newborn screening is part of the "Mother-Child-Pass" examination program. Testing is free of charge, and virtually all newborns (about 80, 000 per year) are tested for an array of inherited metabolic and endocrine diseases. About 80 to 100 children test positive per year.
The implementation of an official advisory board for Austrian newborn screening is an action defined in the Austrian National Plan for rare diseases. Currently, there is no such committee, and relevant issues are usually discussed (on an informal basis) in the working group for inborn errors of metabolism in Austria.

The following (24) diseases are currently part of the programme:

- Hormonal (endocrine) disorders
    - Congenital adrenal hyperplasia

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  - Congenital hypothyroidism
- Amino acidopathies and urea cycle disorders:
  - Phenylketonuria/Hyperphenylalaninämie
  - Tyrosinemia type 1
  - Maple syrup urine disease
  - Arginosuccinic aciduria
  - Homocystinuria
- MAT I/III
  - Citrullinemia
- Organic acidopathies:
  - Methylmalonic aciduria
  - Propionic acidemia
  - Isovaleric acidemia
  - Glutaric aciduria type 1
  - Glutaric aciduria type 2 / Multiple acyl-CoA dehydrogenase deficiency
- Fatty acid oxidation disorders (ß-Oxidation):
  - Medium-Chain-Acyl-CoA dehydrogenase deficiency
  - Very-Long-Chain-Acyl-CoA dehydrogenase deficiency
  - Long-Chain-Acyl-CoA dehydrogenase deficiency
  - Mitochondrial trifunctional protein deficiency
- Disorders of the carnitine cycle:
  - Carnitine palmitoyl transferase 1A deficiency
  - Carnitine palmitoyl transferase II deficiency
  - Carnitine uptake deficiency
  - Carnitine-acylcarnitine translocase deficiency
- Biotinidase deficiency
- Galaktosemia
- Cystic fibrosis

Clinical Practice Guidelines and Training Activities

Clinical Practice Guidelines (CPGs)

Austria has not produced any Clinical Practice Guidelines (CPGs) for Rare Diseases on a national level. A national policy does exist for developing CPGs, but not currently for adoption or implementation of CPGs.

Training and Education

Training on specific Rare Diseases is provided by a number of clinical experts for these diseases; this is also a prerequisite for the official designation as a Centre of Expertise in Austria. One prominent example is the EB (Epidermolysis Bullosa) Academy at the EBhouse in Salzburg.

Information Resources for Rare Diseases

Orphanet Activities

A National Orphanet Team for Austria is operational and based at the Medical University of Vienna, which is a partner of RD-Action. RD-Action will fund the Orphanet team throughout its existence (2015-2018), as no dedicated funding is currently assigned via the National Plan (although Orphanet is mentioned).

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The activities of the Orphanet team are mainly those that are stated as mandatory in the Orphanet SOPs. In addition, Orphanet carried out the nationwide mapping of clinical expertise on rare diseases for the Ministry of Health and Women's Affairs, which is the basis for the identification of further candidates for officially designated Centers of Expertise (this included also collection of data on clinical trials, research projects and registries dedicated to rare diseases).

A similar mapping exercise will be carried out for laboratories specializing in rare disease diagnostics in 2017.

National Helplines

There is no official Rare Diseases helpline operating in Austria, and there are currently no plans to establish one. Only single regional activities have been initiated, by individual rare disease experts, and sustainability is not assured in these cases as they are “in kind” projects.

Official Information Centres

The establishment of the National Coordination Centre for Rare Diseases (CCRD) at the Austrian Health Institute in April 2011, created an information platform for all stakeholders. The CCRD is funded by the Austrian Ministry of Health and Women's Affairs and acts as an information provider in addition to its other functions. The CCRD and Orphanet Austria collaborate closely to allow for maximum synergies between the two structures.

Rare Disease Research Activities

There are currently no specific projects or programmes to fund or facilitate rare disease research in Austria, **although Austria does participate to E-Rare**. The general policy is to fund research based on the quality of individual projects only, rather than to allot a certain budget to RD research. Funding by the major Austrian funding agencies like the Austrian Science Fund (FWF) follows a bottom-up approach, where the quality of the proposal is the sole decision criterion. The FWF is also part of the E-Rare consortium. In addition, there have been specific actions to boost RD research, such as a call by the Austrian National Bank in 2015.

National Alliance of Patient Organisations and Patient Representation

The national alliance of RD patient organizations, ProRare Austria, was founded in December 2011. Between 2014 and 2016 ProRare Austria increased the number of its members to 49 (out of approximately 70 individual patient organizations for rare diseases in Austria) and is continuously strengthening solidarity among its members by linking the different partner organizations.

Since 2014, ProRare Austria has been successfully organizing the annual rare disease day event (including a march with about 400 participants and an indoor event with invited speakers etc.) and was also co-organizer of the EUROPLAN-meeting in Vienna in 2015, as well as the national conference on rare diseases.

Board members of ProRare Austria are also members of the official ‘Expert Committee on Rare Diseases’ of the Austrian Ministry of Health and Women's Affairs. In general, ProRare Austria maintains excellent relationships with all stakeholders within the rare disease field as well as the healthcare system, such as the Austrian Ministry of Health and Women's Affairs, the Main Association of Austrian Social Security Institutions, the Association of the Austrian Pharmaceutical Industry (Pharmig), and academia.

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In 2015/16 ProRare Austria successfully applied for a grant ("Implementation of the measures of the Austrian National Plan for RD", 0.5 FTE for 3 years), which allows for the implementation of several measures of the National Plan, specifically those requiring intense patient input.

Board members of ProRare Austria represent a wide variety of different rare diseases. They have been invited to the main important events in the healthcare arena, e. g. the "Alpbacher Gesundheitsgespräche". By attending meetings with the head physicians of the Austrian Social Security Institutions, ProRare Austria has the possibility to explain and to support the needs of RD patients.

Orphan Medicinal Products (OMPs)

As of November 2015, 91 Orphan Medicinal Products (OMPs) are available in Austria, i.e. are priced and reimbursed or directly provided by the health system. Part of this information is available publicly. Measures are in place to facilitate access to OMPs:

- Compassionate Use Programmes (AV0113 (TRIVAX) Cell based tumor therapy Glioblastoma multiforme)
- OMPs which are not included in the national code of reimbursement can still be reimbursed upon application, if the use of this product is justifiable and essential for the cure of a patient.

There are no incentives to support research into, and the development of (designated or potential) Orphan Medicinal Products

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Main achievements since 2014:

- Establishment of the National Coordination Centre for Rare Diseases, CCRD, (2011) including its two accompanying committees (Expert Committee on Rare Diseases, Strategic Platform), biannual meeting with each committee
- Adoption of the first National Plan for Rare Diseases (NAP.se) in February 2015.
- The Austrian Ministry of Health and Women's Affairs is demonstrating a strong commitment to support the implementation of the measures stated in the NAP.se and has so far been providing continuous funding for the CCRD, the institution coordinating the implementation of the NAP.se.
- Development of a designation process for centres of expertise for rare diseases in Austria by the CCRD (two healthcare providers were involved in the pilot process and will be officially designated in December 2016 and March 2017)
- Nationwide mapping of clinical expertise for rare diseases in order to identify further candidates for official designation as a centre of expertise for rare diseases (close collaboration between Orphanet Austria and the CCRD)
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