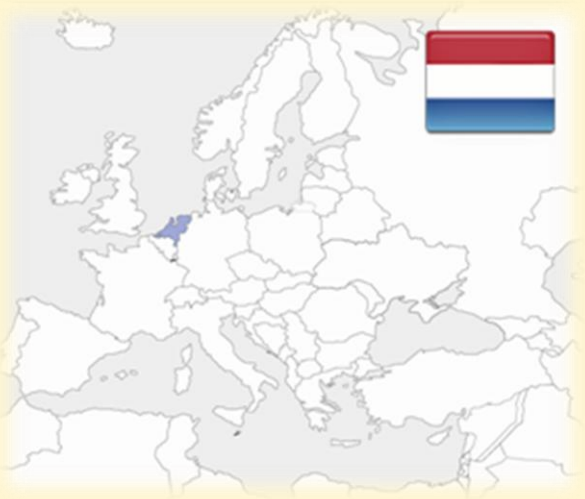
2014 REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE



STATE OF THE ART OF RARE DISEASE ACTIVITIES IN THE NETHERLANDS

This work was financed by the EUCERD Joint Action: Working for Rare Diseases N° 2011 22 01

This document has been produced by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD) Joint Action through the EUCERD Joint Action: Working for Rare Diseases (N° 2011 22 01, Coordinator: Kate Bushby, University of Newcastle, United Kingdom), within the European Union's Second Programme of Community Action in the Field of Health.

The European Union Committee of Experts on Rare Diseases (EUCERD) was established in 2009 and its mandate ended in 2013. It is replaced from 2014 by the Commission Expert Group on Rare Diseases. The EUCERD Joint Action continues to support the activities of the new Expert Group until 2015.

More information on the activities of the former European Union Committee of Experts on Rare Diseases and the EUCERD Joint Action can be found at www.eucerd.eu.

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To quote this document:
Rodwell C., Aymé S., eds., *"2014 Report on the State of the Art of Rare Disease Activities in Europe"*, July 2014.

http://www.eucerd.eu/upload/file/Reports/2014ReportStateofArtRDActivitiesNL.pdf

ACRONYMS

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
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

GENERAL INTRODUCTION

This document 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 European Union Committee of Experts on Rare Diseases (EUCERD) was established in 2009 and its mandate ended in 2013. It is replaced from 2014 by the Commission Expert Group on Rare Diseases. The EUCERD Joint Action continues to support the activities of the new Expert Group until 2015.

The present 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 2013. 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 Commission Expert Group on Rare Diseases. The reader, however, should bear in mind that the information provided is not exhaustive and is not an official position of the European Commission, its Agencies or national health authorities.

The report is split into six parts:

Part I: Overview of rare disease activities in Europe
Part II: Key developments in the field of rare diseases in 2013
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
Part VI: Activities at National level in each EU Member State and other European countries in the field of rare diseases

Parts I – V also include a description of the methodology, sources and validation process of the entire report, and 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 the Netherlands. 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.

Each year, there are around 15 000 downloads of the different sections of the report combined.

RARE DISEASE ACTIVITIES IN THE NETHERLANDS

Definition of a rare disease

Regulation (EC) 141/2000 on orphan medicinal products defines a rare disease: the prevalence of a rare disease is not higher than five per 10,000 individuals. The Netherlands will take no initiatives to amend the definition.

National plan/strategy for rare diseases and related actions

The Health insurance Act is at the basis of the Netherlands' health care system. All patients, including patients with a rare disease, are entitled to diagnosis, care and rehabilitation in line with this Act.

The Minister of Health, Welfare and Sport, Mrs. E. Schippers, sent a letter (with annex) to Parliament on 29 February 2012, in which she expounded the strategy of the Dutch government regarding rare diseases for the years 2012-2015. Some important points in this report are the following:

- Strengthening the role of university hospitals with regard to patient care and research in rare diseases (and centres of expertise);
- Funding (only university hospitals) is designated for care and research;
- Improving reimbursement of orphan medicinal products applied in university hospitals starting 1 January 2012 and in the out-patient setting (starting in 2013). This new policy will not hinder the accessibility of orphan medicinal products;
- The Steering Committee on Orphan Drugs was dissolved (as of 31 December 2011), but stakeholders in the former Steering Committee on Orphan Drugs will assume more tasks and responsibility in their own area of expertise;
- ZonMw (The Netherlands Organisation for Health Research and Development) assume tasks not taken up by the stakeholders that remain from the tasks of the former Steering Committee. The ministry of Health, Welfare and Sport provides funding for the years 2012-2015;
- The Forum Biotechnology and Genetics (also fully subsidised by the ministry of Health, Welfare and Sport) will assume more responsibility on rare diseases and orphan medicinal products;
- A statement on screening.

In addition to this strategy, preparations for a national plan on rare diseases for all stakeholders have started. The Netherlands Organisation for Health Research and Development (ZonMw), has been commissioned by the Ministry of Health, Welfare and Sport to coordinate the input for a National Plan following up on the initial work of the Dutch Steering Committee on Orphan Drugs.

The input of all stakeholders was collected via information from different meetings organised in the last year and via working groups and the website, coordinated by ZonMw/NPZZ and under the auspices of a sounding board especially formed for this task (http://www.npzz.nl/). The website will make public the preparatory documents for the National Plan. In January-March 2012, stakeholders started collecting possible solutions for the issues raised and discussing these on the website and in a public hearing in April 2012. A meeting was organised on 28 August 2012 in Amsterdam to present the first draft of the national plan for rare diseases.

A second draft was presented on the website in January 2013. The National Plan for Rare Diseases received input from all stakeholders and was adopted in October 2013[1] and presented on 10 October 2013 by a delegation of The Netherlands Organization for Health Research and Development (ZonMw) to Minister Schippers of Health, Welfare and Sport (VWS). On 14 November the Minister sent the plan along with her reaction to Parliament. The Dutch National Plan identifies bottlenecks and recommendations, and it encourages field parties to feel responsible. The key bottlenecks for the plan include lack of knowledge about rare diseases, insufficient medical research on causes and course of rare diseases as well as inability of patient organisations to work well together. The plan recommends emphasising knowledge about rare disease through training and establishment of expert centers, make the information widely accessible to diverse audiences; make financial resources available for research and development of treatment as well as maintaining consistent policy for claims and reimbursement of orphan drugs. Finally the plan aims to appoint a director or coordinator to promote all recommendations, and avoid fragmentation and unnecessary duplication within the rare disease field.

[1] http://www.europlanproject.eu/_newsite_986989/Resources/docs/NATIONALPLANS_NETHERLANDS_nl.pdf

Centres of expertise

All stakeholders – and also the government - support the idea that the (follow-up) care and research for patients with rare diseases should be concentrated in, and/or coordinated from, a limited number of centres, in order to guarantee expert care and to stimulate research. In order to stimulate the development of centres of expertise in the Netherlands the Steering Committee on Orphan Drugs developed criteria for expertise centres together with different stakeholders (hospitals, doctors, patients, researchers). These criteria are in line with the criteria established by the EUCERD. The Dutch Government asked the University Medical Centres to work on a plan for concentration of rare disease expertise.

The Dutch Federation of University Medical Centres (NFU) presented their plan at the Conference on the National Plan in August 2012. Here it was stated that the NFU would present their 'list' with centres of expertise early 2013. This list with identified centres will be checked with the information in the Orphanet database and the information collected by the National Patient Alliance for Rare and Genetic Disease (VSOP);

Registries

There is no comprehensive national patient registry in the Netherlands, or designation process, but several patient registries exist for specific rare diseases, including registries maintained by patient organisations and at the main clinical reference centres.

The expertise of several partners involved in the research of rare inborn errors of metabolism (IEM) has been assembled in the Orphan Disease Registry Consortium. Pooling of expertise will greatly support registry of these metabolic diseases in The Netherlands and will lead to improved guidelines for treatment and monitoring as well as a better understanding in the future. This project delivered one thesis in 2012: Fabry disease; studies on diagnosis, screening and patient's perspective. Another result of this project is that the national web-based facilitating registry for inborn errors of metabolism has been further developed[2].

To assist patient organisations in the setting up of patient registries and biobanks, VSOP launched the website www.biobanken.net.

A registry of all patients referred with an abnormal neonatal screening result (NEORAH) has been put into place at the RIVM (National Institute for Public Health and the Environment) for two rare diseases (AGS and sicklecel disease). Furthermore the Netherlands contributes to European registries including ECARUCA, EIMD, TREAT-NMD, AIR, EUROCARE CF, EPCOT, X-ALD and EUROCAT.

Neonatal screening policy

In the current neonatal screening program in the Netherlands 18 rare disorders are diagnosed: phenylketonuria, hypothyroidism, congenital adrenal hyperplasia, cystic fibrosis (2010), biotinidase deficiency, galactosaemia, glutaric aciduria type I, HMG-CoA lyase deficiency, holocarboxylase synthase deficiency, homocystinuria, isovaleric acidemia, maple syrup urine disease, MCAD deficiency, 3-methylcrotonyl-CoA carboxylase deficiency, sickle cell disease, tyrosinemia type I, longchain hydroxyacyl-CoA dehydrogenase deficiency and very-long-chain acyl-CoA dehydrogenase deficiency.

The Dutch Health Council has been asked by the Ministry of Health to present their advice about expanding neonatal screening for other (rare) diseases. Screening is not primarily oriented towards rare diseases, but aimed at those diseases for which some form of treatment is available. In other words establishing a diagnosis in a patient via screening should in theory lead to a gain in health. This can also be the case for rare diseases.

Genetic testing

All eight University Medical Centres are licensed for clinical genetics; to provide counselling and pre- and postnatal testing. Services include genetic counselling, chromosome analysis, biochemical (enzyme) diagnostics and DNA-diagnostics. Genetic counselling is offered locally or in out-clinics affiliated to the centre. All services are offered regionally except for the DNA-diagnostics which, since their start in 1988, operate at a national level. Preimplantation Genetic Diagnosis (PGD) is offered in one University Medical Centre, being connected with several other genetic centres by 'transport PGD'. Patient request for PGD for new genetic indications are seen by both a local and national PGD ethics committee.

All genetic laboratories are accredited according to ISO 15189 (international standard for medical laboratories). Each DNA laboratory provides a specific package of gene tests; tests for the more frequent genetic disorders, like breast cancer are offered by more centres. Tests for rare diseases are usually performed in one laboratory only, but the rare disease diagnostics is in flux due to the application of multigene packages

[2] https://ddrmd.nl/index.php/

for heterogeneous disorders and the emergent application of the whole genome sequencing. Expertise and research is leading in the portfolio of tests offered. Diagnostic tests for 1113 genes and an estimated 1059 diseases are registered in the Orphanet database[3].

Genetics services in the Netherlands are funded by the private health insurance companies through a special budget. Diagnostic tests are reimbursed on the condition that there is a medical reason to do this test. For tests that are not available in the Netherlands, samples can be sent abroad. Molecular genetic laboratories have distributed the tests according to specific expertise that is available.

National alliances of patient organisations and patient representation

VSOP is the Dutch national alliance of patient organisations for rare and genetic disease, representing 67 of such organisations in The Netherlands (www.vsop.nl). VSOP deals with specific, mutually shared issues related to rare and genetic disease in health care policy; perinatal care, including preconception care; biomedical research; prevention; standards of care; orphan medicines, paediatric medicine, ethical and societal issues. VSOP works in partnership with other Dutch patient umbrella organisations (NPCF, CG-Raad, PlatformVG) that are dealing with issues that may also effect people with rare disorders.

VSOP has an equal voice in several national governmental bodies dealing with health care and research policy relevant to rare diseases: the Dutch Health Council (Gezondheidsraad), the national PGD committee, the RIVM prenatal and neonatal screening committees, the Forum Biotechnology and Genetics, ZonMw, CBG advanced therapy committee, etc. VSOP works in partnership with both member and non-member patient organisations to improve quality of care, quality of life and to stimulate research. With regards to the designation of centres of expertise, VSOP works together with Orphanet and the umbrella of academic medical centres (NFU) to bring in the patient perspective and stimulate quality and cooperation. VSOP actively participates in the development and future implementation of the Dutch National Plan for Rare Diseases.

Most disease specific organisations in The Netherlands, including organisations for rare diseases, receive between €25,000 and €35,000 governmental funding per year. The VSOP was successful in the acquisition of project grants from other sources, like governmental funds, charities and EU-funded programs, making it possible to have about 15 employees working for the quality of life of people with rare and genetic diseases and their families. However, the structural governmental funding of VSOP will end in 2014.

In addition the VSOP and all other patient organisations receive vouchers, worth €18,000, to be combined with 6 other vouchers (patient organisations) to realize patient-driven projects. In total 18 projects started with 201 vouchers from patient organisations. Three vouchers projects where specifically dedicated to rare diseases, with a total budget of €1.5 million

VSOP has a strong European and international orientation. It represents the European patient umbrella EURORDIS in The Netherlands and participates on behalf of EGAN (www.egan.eu) in several European projects (e.g. Gencodys, GRIP, ECRIN-IA, EUPATI, Europlan, and currently in negotiation: Asterix and Closed) and committees, like the COMP at EMA, London and the ESHG Quality Committee. VSOP also initiated 'Preparing for life' an international strategy for preconception care. In 2012, cooperation in this field started with WHO.

Sources of information on rare diseases and national help lines

Orphanet activities in the Netherlands

Since 2004, there is a dedicated Orphanet team in the Netherlands, currently hosted by the Leiden University Medical Centre. The Leiden University Medical Centre was designated by the Ministry of Health, Welfare and Sport in 2010 as the official Orphanet team for the Netherlands. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, bio banks, clinical trials and patient organisations) in their country for entry into the Orphanet database. The team also manages the Orphanet Netherlands[4] national website in Dutch which was launched in 2011.

A collaboration has been established between Orphanet and the Erfocentrum, the Dutch National Genetic Resource and Information Centre. Erfocentrum provides information about genetic diseases to the Dutch general public and for that purpose it has written Dutch abstracts for approximately 500 rare genetic diseases. All of these abstracts are validated by clinical geneticists and patient organisations. This collaboration allows Orphanet to use the Erfocentrum abstracts to provide information about rare diseases to the Dutch-speaking public. Hyperlinks, leading to the Erfocentrum website containing the Dutch abstracts, will be added to the disease-pages on Orphanet.

[3] Data extracted from orphanet in January 2014.

[4] http://www.orpha.net/national/NL-NL/index/homepage/?lng=FR

Starting February 2012, the entry of new specialised Dutch clinics in the Orphanet database is validated by the Scientific Advisory Board of Orphanet the Netherlands. Being represented in this board, VSOP contacts patient organisations to give their perspective on applications of (candidate) centre, using the EUCERD criteria.

Official information centre for rare diseases

As of 31 December 2011, the Steering Committee was disbanded by the government: however ZonMw (the Netherlands Organisation for Health Research and Development) was stimulated to install a general information desk at the secretariat for rare diseases with as main objective to coordinate the plan on RD (NPZZ). With a small financial incentive (€30 000) ZonMw has stimulated the development of new information portals for researchers and small pharmaceutical companies about orphan drugs. After this project this portal should be embedded within the Dutch Pharmaceutical Umbrella Organisations: Biofarmind and Nefarma.

Help line

The most used help line for rare disorders is the Erfocentrum ERFO line, providing information on genetic and rare diseases and pregnancy/reproduction related questions. This line can be reached by phone and e-mail.

The Royal Dutch Association of Pharmacists (KNMP) has developed in collaboration with the Steering Committee on Orphan Drugs the website www.farmanco.knmp.nl/weesgeneesmiddelen which publishes practical information on European registered orphan medicinal products, in particular for pharmacists but patients can also make use of it.

Information on neonatal screening is available from the National Institute for Public Health and the Environment (RIVM)[5], both for the general public, parents and physicians. Information is also provided by the many Dutch patient organisations, pharmaceutical companies and the Federation of University Hospitals, etc.

Other sources of information on rare diseases

The website www.erfelijkheid.nl contains a database of approximately 500 rare diseases with information for both lay-persons and professionals. In 2013, 50 new rare diseases (all chromosome disorders) were added to the database. In addition, public information is available on genetic, biomedical and pregnancy related issues[6]. Since 2010 videos were added to the website. In 2012 ten new videos were produced and added. Using videos, disease characteristics can be visualised in order to improve the dissemination of information for both patients and medical professionals.

While www.erfelijkheid.nl is successfully reaching an audience of patient, their family and the general public, Erfocentrum also participates in the website www.huisartsengenetica.nl, which focuses on general practitioners. Erfocentrum also provides news on genomics and rare diseases via email to more than 100 patient organizations and via Twitter to over 400 medical professionals and organisations.

Guidelines

VSOP hosts a website dedicated to good practice guidelines for rare diseases. On this website, www.zorgstandaarden.net, standards of care for rare diseases developed by VSOP are published, to be used by healthcare providers. Both generic themes and disease-specific standards are worked out. In addition, in 2012 VSOP finished 33 treatment guidelines for general practitioners carried out in close collaboration with the related patient organisations and the Dutch College of General Practitioners (NHG). Ten additional guidelines are in preparation.

Clinical guidelines on mitochondrial diseases and on Guillain-Barré syndrome (GBS) were launched in 2012. The alliance for Neuromuscular Diseases developed in cooperation with medical specialists specific information for GBS which patient can take with them (to the GP and others), in line with the project 'Patient as information carrier'. The patient organisation VKS (Adults, Children and Metabolic disorders) developed 20 new healthcare pathways for metabolic diseases.

Training and education initiatives

At governmental level, training and education initiatives in the field of rare diseases are not foreseen, because these are the remit of universities and professional organisations. The Boerhaave Committee (at Leiden University Medical Centre) organises the annual Princess Beatrix Fund Symposium on Neuromuscular Diseases

[5] www.rivm.nl/pns/hielprik

[6] These sites provide further web based information: www.biomedisch.nl; www.zwangernu.nl; www.zwangerwijzer.nl; www.slikeerstfoliumzuur.nl; www.prenatalescreening.nl

for medical specialists and their assistants. There is still a growing interest at college and university students to write a paper on rare diseases or orphan medicinal products.

Training for health care providers on prenatal and neonatal screening is organised at a regular basis by the National Institute for Public Health and the Environment. Documents used in training are available at the website[7].

National rare disease events in 2013

On 2 March[8], events for Rare Disease Day were organised by ZonMw, Genzyme and VSOP. A gathering of over 300 adults and children was organised in Utrecht to serve as inspiration to promote research and better care for rare diseases. The children enjoyed creative and cultural programs, while adults participated in an informative meeting. In addition, the annual Angel Awards were also handed out.

A Europlan National Conference was held on 14 &15 November 2013 in The Hague, co-organised by VSOP and Eurordis with the aim of exploring the provisions and implementation of the newly published Plan for Rare Diseases.

Hosted rare disease events in 2013

Amongst the rare disease events announced in OrphaNews Europe were: 3rd European Rett Syndrome Conference Maastricht, "Research Update & Preventive Management" (17-19 October 2013, Maastricht), 6th International Conference on Children's Bone Health (22-25 June 2013, Rotterdam).

Research activities and E-Rare partnership

National research activities

A multi-annual research programme started in 2011 at The Netherlands Organisation for Health Research and Development (ZonMw) with a funding of €13.4 million. The main objective of this is to stimulate translational research in rare diseases with the aim of developing therapies. Three projects were each awarded a €3 million grant under this ZonMw Priority Medicines for Rare Diseases and Orphan Drugs (PM Rare) research programme[9]. The projects involve research that could potentially lead to new therapies for rare diseases and are to be carried out by public-private partnerships. Those selected are: antisense therapy for several major rare diseases; gene-corrected stem cells for curative treatment of severe combined immunodeficiency; and towards treatment of MELAS syndrome: drug development based on newly identified compounds.

ZonMw, the Netherlands Organisation for Health Research and Development, funds health research and stimulates use of the knowledge developed to help improve health and healthcare in the Netherlands. ZonMw's main commissioning organisations are the Ministry of Health, Welfare and Sport and the Netherlands Organisation for Scientific Research. Within several ZonMw programmes, RD research is financed (e.g. Efficacy research OD, Stem cell and Gene therapy, HTA, screening)[10]

There are tax reductions for R&D in high-tech start-ups from which orphan medicinal product companies can benefit. There are also several programmes from the Ministry of Economic Affairs to facilitate start-ups and SME's (Innovation Fund) that orphan medicinal product companies can benefit from.

In 2011, the Netherlands Organisation for Scientific Research made €22.5 million available to a consortium including 8 Dutch University Medical Centres and other research institutes and universities in order to establish a national biobanking infrastructure, the Biobanking and Biomolecular Resources Research Infrastructure Netherlands (BBMRI-NL), which will integrate clinical materials and data gathered over many years with the goal of improving access to human samples. Such samples are important to rare disease and orphan medicinal product research. In 2011, 26 new projects started. In the databank are (October 2012) 191 Dutch Biobanks and over 500 000 participants. In 2013 new projects will be able to be granted.

The VU University Medical Centre in Amsterdam is working together with the Dutch Neuromuscular Diseases Association in the development of an n-of-1 trial service. The project investigated whether such trial treatments, to be facilitated by the n-of-1 trial service, could be reimbursed by the Dutch basic health insurance. It is also examining whether the results of this type of research may be sufficient for authorities to decide on the effectiveness of an off-label medicine and its reimbursement for future patients with the rare disease in question.

[7] For instance information for screeners and information on the diseases screened: www.rivm.nl/pns/hielprik/films.
[8] www.zeldzameziektendag.nl
[9] http://www.zonmw.nl/nl/programmas/programma-detail/priority-medicines-zeldzame-ziekten-en-weesgeneesmiddelen-rare/algemeen/
[10] http://www.zonmw.nl/nl/themas/thema-detail/zeldzame-ziekten-en-weesgeneesmiddelen/thema-detail/

Participation in European research projects
Dutch teams participate (or participated) in 102 FP7 rare disease related projects and are also coordinators of 21 projects.

E-Rare
The Dutch Organisation for Health Research and Development (ZonMw) participates in E-Rare 1 (2006-2010) and E-Rare 2 (2010-2014), and participated in the 4th Joint Transnational Call in 2012: teams from the Netherlands participate in 8 out of the 11 consortia selected for funding. In 2013, ZonMw did not participate in the 5th Joint Transnational Call.

IRDiRC
The Netherlands Organisation for Health Research and Development (ZonMw) and the pharmaceutical enterprise Prosensa are committed members of the IRDiRC.

Orphan medicinal products
Orphan medicinal product committee[11]
In 2011 the Steering Committee focused on the draft for a national plan in close cooperation with different stakeholders. However, it was decided that the Steering Committee would not be funded by the Dutch government after December 2011 and no longer existed as a governmental committee from 2012 onwards. Stakeholders in the former Steering Committee on Orphan Drugs will assume more tasks and responsibility in their own area of expertise in the future with the Netherlands Organisation for Health Research and Development ZonMw taking more responsibility and assuming a number of tasks from the former Steering Committee. Notably, the coordination of the development and implementation of a national strategy will be from 2012 onwards assumed by a secretariat at ZonMw and the sounding board on the National Plan. This plan will not only cover Orphan Drugs but also Rare Diseases.

Orphan medicinal product incentives
A waiver can be granted for the registration fee of a medicinal product if the medicinal product is already registered in one or several other EU member states and if the prevalence of the indicated disease is less than 1 in 200.000 inhabitants in the Netherlands. In the case of orphan medicinal products for a rare disease for which no alternative treatments exist, there is no obligation for companies to provide pharmacoeconomic data. In individual cases this may also be the case for orphan medicinal products for a disease with a prevalence no more than 5 persons per 10,000 for which an alternative treatment does exist.

The programme for Expensive and Orphan Medicines (2007-2014) aims to investigate the effectiveness of expensive drugs and of expensive orphan medicinal products and the development of HTA methodology to help the Dutch Health Care Insurance Board in its advice on reimbursement. In the scope of this programme, several projects on registered orphan medicinal products have already been selected. As of 1 January 2009, the subsidy scheme Orphan Designation Dossier (ODD) is in action. This is an initiative of the Dutch Steering Committee on Orphan Drugs and is executed by the Netherlands Organisation for Health Research and Development (ZonMw). This initiative will help stimulate the development of orphan medicinal products in the Netherlands by providing Dutch pharmaceutical Small and Medium-sized Enterprises (SMEs) a small subsidy for the costs of writing and submitting the ODD to the EMA.

Orphan medicinal product market availability situation
In the Netherlands, all orphan medicinal products with EU market authorisation are available on the market. The government decides which of the products will be reimbursed. Therefore it is necessary to file a reimbursement dossier at the Dutch Health Care Insurers Board (CVZ), the advisory body concerning reimbursement. If there is no registered drug for a rare disease, the treatment can be paid for if the disease is very rare (less than 1 in 150 000 inhabitants) and there no other alternative and there is scientific evidence about using the drug for the specific disease. Costs are covered by the health insurer, the health care insurance company can obtain scientific advice at CVZ about evidence.

Orphan medicinal product pricing policy
The minister will start the negotiation with pharmaceutical companies about pricing *(see evaluation of conditional reimbursement in the section below).*

[11] Also the former Dutch Steering Committee OD had a broader assignment than only OD

Orphan medicinal product reimbursement policy

In the Netherlands the following orphan medicinal products are reimbursed: Aldurazyme, Arzerra, Carbaglu, Cayston, Cystadane, Diacomit, Elaprase, Evoltra, Exjade, Fabrazyme, Firdapse, Glivec, Increlex, Kuvan, Lysodren,Mepact, Myozyme, Naglazyme, Nexavar, Nplate, Orfadin, Prialt, Replagal, Revatio, Revlimid, Revolade, Signifor, Siklos, Soliris, Somavert, Sprycel, Tasigna, TOBI podhaler, Torisel, Tracleer, Ventavis, Vidaza, Volibris, Votubia, Wilzin, Xagrid, Yondelis, Zavesca.

The following orphan medicinal products are available when ordered by a physician or a pharmacist either through a hospital budget or on a named-patient basis: Atriance, Busilvex, Ceplene, Esbriet, Firazyr, Gliolan, Inovelon, Litak, , Mozobil, Pedea, Photobarr, Peyona, Plenadren, Rilonacept Regeneron, Savene, Tepadina, Thalidomide, Trisenox, , VPRIV and Vyndaquel.

In 2012, the Dutch Health Care Insurance Board (CVZ) addressed the country's Minister of Health concerning the conditional reimbursement of three rare disease products deemed "too expensive". These products target lysosomal storage disorders: a treatment for Pompe disease and Fabry disease treatment. Health Minister Edith Schippers has been advised to cut public funding for the treatments, although babies diagnosed with Pompe disease would continue to have their treatment supported by State funding under the proposal. The minister will start the negotiation with pharmaceutical companies about pricing. During this negotiation the drugs were reimbursed from 2013.

Other initiatives to improve access to orphan medicinal products

A physician may prescribe non-authorised drugs (e.g. drugs, including orphan medicinal products, authorized elsewhere or even not authorised anywhere), but only with an approval of the Health Inspectorate. The prescribed drug is not reimbursed, unless the health insurer chooses to do so. Apart from these provisions, there are no other initiatives regarding access.

Other therapies for rare diseases

No specific information reported.

Orphan devices

There are no (new) initiatives regarding orphan devices.

Specialised social services

Respite care services are available, imbedded in the general health care system.

DEVELOPMENT OF RARE DISEASE ACTIVITIES IN 2013 IN THE NETHERLANDS

National plan/strategy for rare diseases and related actions

The National Plan for Rare Diseases was adopted in October 2013[12] and presented on 10 October 2013 by a delegation of The Netherlands Organization for Health Research and Development (ZonMw) to Minister Schippers of Health, Welfare and Sport (VWS). On 14 November the Minister sent the plan along with her reaction to Parliament. The Dutch National Plan identifies bottlenecks and recommendations, and it encourages field parties to feel responsible. The key bottlenecks for the plan include lack of knowledge about rare diseases, insufficient medical research on causes and course of rare diseases as well as inability of patient organisations to work well together. The plan recommends emphasising knowledge about rare disease through training and establishment of expert centers, make the information widely accessible to diverse audiences; make financial resources available for research and development of treatment as well as maintaining consistent policy for claims and reimbursement of orphan drugs. Finally the plan aims to appoint a

[12] http://www.europlanproject.eu/_newsite_986989/Resources/docs/NATIONALPLANS_NETHERLANDS_nl.pdf

director or coordinator to promote all recommendations, and avoid fragmentation and unnecessary duplication within the rare disease field.

Sources of information on rare diseases and national help lines

Other sources of information on rare diseases

website www.erfelijkheid.nl contains a database of approximately 500 rare diseases with information for both lay-persons and professionals. In 2013, 50 new rare diseases (all chromosome disorders) were added to the database. In addition, public information is available on genetic, biomedical and pregnancy related issues[13]. Since 2010 videos were added to the website. In 2012 ten new videos were produced and added. Using videos, disease characteristics can be visualised in order to improve the dissemination of information for both patients and medical professionals.

While www.erfelijkheid.nl is successfully reaching an audience of patient, their family and the general public, Erfocentrum also participates in the website www.huisartsengenetica.nl, which focuses on general practitioners. Erfocentrum also provides news on genomics and rare diseases via email to more than 100 patient organizations and via Twitter to over 400 medical professionals and organisations.

National rare disease events in 2013

On 2 March[14], events for Rare Disease Day were organised by ZonMw, Genzyme and VSOP. A gathering of over 300 adults and children was organised in Utrecht to serve as inspiration to promote research and better care for rare diseases. The children enjoyed creative and cultural programs, while adults participated in an informative meeting. In addition, the annual Angel Awards were also handed out.

A Europlan National Conference was held on 14 &15 November 2013 in The Hague, co-organised by VSOP and Eurordis with the aim of exploring the provisions and implementation of the newly published Plan for Rare Diseases.

Hosted rare disease events in 2013

Amongst the rare disease events announced in OrphaNews Europe were: 3rd European Rett Syndrome Conference Maastricht, “Research Update & Preventive Management” (17-19 October 2013, Maastricht), 6th International Conference on Children's Bone Health (22-25 June 2013, Rotterdam).

Research activities and E-Rare partnership

E-Rare

In 2013, ZonMw did not participate in the 5th Joint Transnational Call.

[13] These sites provide further web based information: www.biomedisch.nl; www.zwangernu.nl; www.zwangerwijzer.nl; www.slikeerstfoliumzuur.nl; www.prenatalescreening.nl

[14] www.zeldzameziektendag.nl

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SELECTED BIBLIOGRAPHY AND SOURCES[16]

- Dutch Organisation for Health Research and Development (ZonMw)/ NPZZ http://www.zonmw.nl/en/
- National Plan Rare Diseases (NPZZ) website http://www.npzz.nl/
- National Plan Rare Diseases (NPZZ)

[15] 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.
[16] All websites and documents were last accessed in May 2014.

http://www.europlanproject.eu/_newsite_986989/Resources/docs/NATIONALPLANS_NETHERLANDS_nl.pdf

- National Genetic Resource and Information Centre
  http://www.erfocentrum.nl
- Orphanet Netherlands national website
  http://www.orpha.net/national/NL-NL/index/homepage/?lng=EN
- Forum Biotechnologie en Genetica
  http://www.forumbg.nl/documenten
- Farmanco – List of Orphan Drugs registered in the European Union (in Dutch)
  http://www.farmanco.knmp.nl/tekortweesgeneesmiddel
- VSOP
  http://www.vsop.nl/
- Rare Disease Day
  www.zeldzameziektendag.nl
- List of genetic diagnostic tests in Netherlands
  http://www.dnadiagnostiek.nl/
- Europlan Dutch National Conference Final Report
  http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_netherlands_%20europlan.pdf