

**2012 REPORT ON THE STATE OF THE ART
OF RARE DISEASE ACTIVITIES IN EUROPE
OF THE
EUROPEAN UNION COMMITTEE OF EXPERTS
ON RARE DISEASES**



**STATE OF THE ART OF RARE DISEASE ACTIVITIES IN
BULGARIA**

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, formerly the European Commission's Rare Diseases Task Force) 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.

More information on the European Union Committee of Experts on Rare Diseases can be found at www.eucerd.eu.

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To quote this document:

Aymé S., Rodwell C., eds., "2012 Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases", July 2012.

ISBN : 978-92-79-25355-3

DOI : 10.2772/50554

<http://www.eucerd.eu/wp-content/uploads/2012/09/2012ReportStateofArtRDActivitiesBG.pdf>

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ACRONYMS

General

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 (Iceland, Switzerland, Norway)
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

Pilot European Reference Networks

Dyscerne - European network of centres of expertise for dysmorphology
ECORN-CF - European centres of reference network for cystic fibrosis
Paediatric Hodgkin Lymphoma Network - Europe-wide organisation of quality controlled treatment
NEUROPED - European network of reference for rare paediatric neurological diseases
EUROHISTIONET - A reference network for Langerhans cell histiocytosis and associated syndrome in EU)
TAG - Together Against Genodermatoses – improving healthcare and social support for patients and families affected by severe genodermatoses
PAAIR - Patients' Association and Alpha-1 International Registry Network
EPNET - European Porphyria Network - providing better healthcare for patients and their families
EN-RBD -European Network of Rare Bleeding Disorders
CARE-NMD -Dissemination and Implementation of the Standards of Care for Duchenne Muscular Dystrophy in Europe project
ENERCA - European network for rare and congenital anaemia – Stage 3

GENERAL INTRODUCTION TO THE REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE OF THE EUROPEAN UNION COMMITTEE OF EXPERTS ON RARE DISEASES

The 2012 Report on the State of the Art of Rare Disease Activities in Europe 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 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 2011. 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 European Union Committee of Experts on Rare Diseases. The reader, however, should bear in mind that the information provided is not exhaustive and is not an official position of either the European Commission, its Agencies or national health authorities.

The report is split into five parts:

Part I: Overview of rare disease activities in Europe

Part II: Key developments in the field of rare diseases in 2011

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

Each part contains a description of the methodology, sources and validation process of the entire report, and concludes with 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 Bulgaria. 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 report¹.

¹ <http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArRDActivities.pdf>

RARE DISEASE ACTIVITIES IN BULGARIA

Definition of a rare disease

Stakeholders in Bulgaria accept the definition of a prevalence of no more than 5 in 10'000 individuals. This definition is officially mentioned in the Bulgarian National Plan for Rare Diseases.

National plan/strategy for rare diseases and related actions

On 27 November 2008, the Bulgarian Council of Ministers approved the National Plan for Rare Diseases – genetic disorders, congenital malformations and nonhereditary diseases (2009 – 2013). The Bulgarian National Plan for Rare Diseases started on 1 January 2009 and will last for 5 years. Bulgaria's National Plan for Rare Diseases is currently active and consists of nine priorities targeting all rare diseases:

- Collection of epidemiological data for rare diseases in Bulgaria by creation of a national register;
- Improvement of the prevention of genetic rare diseases by enlarging the current screening programmes;
- Improvement of the prevention and diagnostics of genetic rare diseases by introducing new genetic tests, decentralisation of the laboratory activities and easier access to medico-genetic counselling;
- Integrative approach to the prevention, diagnostics, medical treatment and social integration of patients and their families;
- Promotion of the professional qualification of medical specialists in the field of early diagnostics and prevention of rare diseases;
- Feasibility study on the necessity, possibility and criteria for the creation of a reference centre for rare diseases of functional type;
- Organisation of a national campaign to inform society about rare diseases and their prevention;
- Support and collaboration with NGOs and patient associations for rare diseases;
- Collaboration with the other EU members.

A National Consulting Council on Rare Diseases has been established by the Ministry of Health, and meets once a month to supervise the progress and implementation of the plan: the Council includes medical professionals, Ministry representatives and a representative of the National Alliance of People with Rare Diseases. Although the estimated budget of the Plan is €11.3 million, the assigned funds are much less and are disproportionately distributed (i.e. directed towards genetic testing activities). The estimated budget does not envisage take into account the costs for the provision of clinical services for rare disease patients. Funding for rare disease policies is provided by the Ministry of Health and reimbursements of drugs for rare diseases are covered by the Ministry of Health (defined by Ministerial Ordinance 34) and the National Health Insurance Fund (defined by Ministerial Ordinance 38). Since 2011 there has been a tendency to gradually transfer all rare diseases treatment coverage from the Ministry of Health to National Health Insurance Fund. However, the Ministry of Health stays a major actor in rare diseases treatment provision through the Ministry of Health-operated Fund for Children's Treatment and Commission for Treatment Abroad.

In addition to these measures, the First National Conference for Rare Diseases in Bulgaria (28 to 30 May 2010)², organised within the scope of the EUROPLAN project, brought together stakeholders in order to discuss the provisions of the plan and its implementation. The conference participants agreed on the following general proposals and guidelines for actions at national level: to fully support of the priorities set out in the EU Council Recommendation on an action in the field of rare diseases adopted on 8 June 2009; to secure the implementation of the Bulgarian National Programme for rare diseases with the appropriate funds as defined in the budget framework; to stress the need for urgent legislative initiatives to protect the rights of people with rare diseases and to ensure the adequate prevention, treatment, rehabilitation and social cares; to encourage the establishment of epidemiological registries for rare diseases in Bulgaria; to implement of an integrated approach to people with rare diseases and their families; to organise a public campaign to fund and stimulate research on rare diseases in Bulgaria. The final report of the workshop has been published and is available online for public consultation³.

² <http://www.conf2010.raredis.org/>

³ http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/FINAL%20Report_Bulgaria_n%20EUROPLAN%20NC%202010%20-%20Report%20Package.pdf

Centres of expertise

Currently, there is no official designation procedure for centres of expertise for rare diseases in Bulgaria. The national plan will carry out a feasibility study on the necessity, possibility and criteria for the creation of a centre of expertise for rare diseases. However, there are several academic centres that are specialised as centres of research, treatment and management for rare diseases, i.e. cystic fibrosis, mucopolysaccharidosis, thalassemia major, Gaucher disease and neuromuscular diseases. Treatment with orphan medicinal products is currently reimbursed in these centres, which also manage the provision of very expensive orphan medicinal products. Medical experts from these centres also participate in developing protocols for the National Health Insurance Fund, which serve the treatment of rare disease patients. The requirements and criteria for the designation of centres of expertise are under discussion: it is expected that these centres would be located within university hospitals. The envisaged network will include 5-6 centres at national level: the centres will be equally distributed geographically throughout the country and will deal with all rare diseases.

In addition to these measures, since May 2009, the Bulgarian Association for Promotion of Education and Science runs highly specialised medical centre for rehabilitation and education of people with rare diseases "RareDis". The main idea is to upgrade the services of the Information Centre for Rare Diseases and Orphan Drugs, by launching a tertiary-level rehabilitation centre, aimed at improving the quality of life of people with rare diseases.

Pilot European Reference Networks

Bulgaria participates, or has participated, in the following European Reference Networks for rare diseases: Dyscerne and Care-NMD.

Registries

Seven nation-wide epidemiological registries concerning rare diseases have been identified: the National Registry of Patients with Thalassemia Major, the National Registry of Chronic Myeloid Leukaemia Patients, the National Registry of Crohn Disease Patients, the National Registry of Wilson Disease Patients, the National Registry of Gaucher Disease Patients, the National Registry of Mucopolysaccharidosis type 2 Patients and the the National Cancer Registry.

On 28 October 2009, BAPES (Bulgarian Association for the Promotion of Education and Science) was officially given the status of data privacy administrator of rare diseases registries by the Commission for Protection of Data Privacy. Soon after, the collection of epidemiological data for the project "The National registry of thalassaemia major patients in Bulgaria" started. The project is implemented as a result of the common work and cooperation between BAPES, ICRDOD, Medical Centre "RareDis", Bulgarian Scientific Society of Clinical and Transfusion Haematology, university haematology clinics and thalassaemia patient organisations. A subsequent update and collection of new epidemiological data was organised in March-April 2011, results of Phase III were published in June 2011⁴.

Following this very successful model, BAPES has initiated recently 5 new rare diseases registries. In May 2011 the first results from a joint study of BAPES and Wilson disease patient association were published⁵. The Crohn Disease National Registry is already working and its first statistics⁶ were officially adopted in June 2011 at a Crohn Disease national workshop. The Bulgarian Scientific Society of Gastroenterology, Gastrointestinal Endoscopy and Abdominal Echography and the university gastroenterology clinics throughout the country have greatly supported and contributed to both Crohn and Wilson patient registries. Just before the Second National Conference for Rare Diseases in September 2011 the provisional results of two new rare diseases patient registries were announced for Gaucher disease and Mucopolysaccharidosis type 2. The corresponding patient associations have provided data, which were analysed by BAPES. In December 2011 BAPES has reached agreements with the Bulgarian Scientific Society for Clinical and Transfusion Haematology and the Bulgarian Scientific Chirurgic Society for launching two new rare diseases registries for primary myelofibrosis and neuroendocrine tumors respectively. A unique character of all BAPES-managed epidemiological registries for rare diseases is that they involve joint activities by all relevant stakeholders.

Some rare tumours are included in the National Cancer Registry, which receives public (governmental) funding.

Bulgaria also contributes to the EUROCARE CF and TREAT-NMD European registries.

⁴ http://www.raredis.org/?page_id=2432&mel=4&smel=41&lang=en

⁵ http://www.raredis.org/?page_id=2447&mel=4&smel=44&lang=en

⁶ http://www.raredis.org/?page_id=2454&mel=4&smel=43&lang=en

Neonatal screening policies

One of the national plan's priorities is to improve the availability and accessibility of the current screening programs. In 1979 mass neonatal screening was introduced in Bulgaria for phenylketonuria, galactosaemia (discontinued in 1993), congenital hypothyroidism and congenital adrenal hyperplasia. Some selective metabolic screening programmes are coordinated by the University Maternity Hospital National Genetic Laboratory in Sofia for the metabolic screening programmes (phenylketonuria), and the University Paediatric Hospital in Sofia for the endocrine screening programmes (congenital hypothyroidism and congenital adrenal hyperplasia). There is logistic coverage of the entire country with more than 130 neonatal structures carrying out blood sampling 3-5 days after birth. Over 90% of neonates are included in existing measures. Ordinance Nr.26 2007 of the Bulgarian Ministry of Health provides equal access to the neonatal screening programmes. However, there exist certain problems, such as postponed mailing of screening cards to centralised labs, and the need for technological upgrades.

Genetic testing

Genetic tests for the diagnosis of rare disorders are provided mainly by the National Genetic Laboratory (NGL). This organisation was established more than 35 years ago, by initiating of biochemical analysis for some rare disorders and mass neonatal screening for PKU. At the moment NGL provides routine diagnosis with DNA analysis (including prenatal and evaluation of carrier status) for many disorders: cystic fibrosis, phenylketonuria, Wilson disease, neuromuscular disorders, Niemann–Pick (in target population), beta thalassemia, galactokinase deficiency (in target population), microdeletions and microduplications syndromes, inborn hypothyroidism and other. The NGL also has the capacity to perform routine enzymatic analysis and GS/MS analysis for diagnosis of many rare disorders (Krabe, Pompe, MPS). In 2010 the laboratory introduced MS/MS analysis for metabolic study of inherited disorders.

The government organises support of testing by financing diagnostic kits and consumables. Genetic testing abroad is possible for diseases for which the genetic test is not available in Bulgaria, after commission approval.

Diagnostic tests are registered as available in Bulgaria for 34 genes and an estimated 40 diseases in the Orphanet database⁷.

National alliances of patient organisations and patient representation

The National Alliance of People with Rare Diseases (NAPRD) in Bulgaria is an umbrella organisation of around 30 rare disease patient associations and single members with rare diseases not represented by an association. It aims to create a link between the people with rare diseases and the representatives of the social and healthcare system. The Alliance works for the right to timely and equal medical care. The organisation also lobbies for the creation of adequate laws in the field of the protection of the rights of the people with rare diseases.

Public funding is available for nation-wide patient organisations in Bulgaria. Patient representatives are members of the management board of the National Health Insurance Fund, the committee for transparency at the Ministry of Health and the national consultative committee on rare diseases.

Sources of information on rare diseases and national help lines

Orphanet activities in Bulgaria

Since 2004 there is a dedicated Orphanet team in Bulgaria, currently hosted by the Information Centre for Rare Diseases and Orphan Drugs (ICRDOD). This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

Official information centre for rare diseases

ICRDOD⁸ is a project and activity of the Bulgarian Association for Promotion of Education and Science (BAPES⁹) - a non-government non-profit organisation, registered under the Bulgarian law on non-profit legal in 2003. ICRDOD is a free educational and informative service in Bulgarian and English, providing personalised replies to requests from patients, families and medical professionals. It operates a multilingual website (www.raredis.org) and a rare disease help line - (+359) 32 57 57 97.

⁷ Information extracted from the Orphanet database in September 2011.

⁸ <http://www.raredis.org/>

⁹ http://www.raredis.org/?page_id=2147&mel=8&smel=81&lang=en

In 2010 ICRDOD started publishing reviews on rare diseases topics. These papers' objective is to summarise important information on particular topics in the field and to present it in a reader-friendly format.

ICRDOD published in March 2011 an updated review of the access to orphan medicinal products for rare diseases in Bulgaria¹⁰: the report contains 4 sections: orphan medicinal product designation and marketing authorisation; pricing, inclusion in the Positive drug list and reimbursement; mechanisms for accelerated access to innovative medicines; conclusions. There are 2 annexes, attached to the review: list of orphan medicinal products in EU and Bulgaria, which contains information about the trade name, ATC code, active substance, indication(s), marketing authorisation holder and date of marketing authorisation for each item (additionally, it is indicated whether the drug is present in the Positive drug list of Bulgaria and if it is reimbursed by public funds); and a list of references.

A review of rare diseases patient registries in Bulgaria is currently under preparation.

The ICRDOD site was substantially renewed and upgraded at the end of 2011. Besides a new look and new layout of content, the site offers several new features for its users, such a subscription for its newsletter "Rare Diseases & Orphan Drugs", an online registry of rare diseases patients, an updated Rare Diseases Library in Bulgarian, as well as better interaction between the different users and ICRDOD team.

Since December 2010 ICRDOD publishes a newsletter¹¹ on a bi-monthly basis. It focuses recent advances and news, concerning all rare diseases stakeholders. Every issue contains a cover story with an interview, news and announcements and a rare diseases reading list. It is electronic and distributed free of charge. The newsletter is published in two versions – Bulgarian (ISSN 1314-3581) and English (ISSN 1314-359X).

Help line

ICRDOD provides a rare disease help line - (+359) 32 57 57 97 providing personalised replies to requests from patients, families and medical professionals. ICRDOD is a member of EURORDIS-led European Network of Rare Diseases Help Lines and took part in the Network's Caller Profile Analysis 2011.

Other sources of information

Departments of Medical Genetics at all University Hospitals and the National Genetic Laboratory also provide information.

Good practice guidelines

Several national best practice guidelines are available in Bulgaria, for example the guidelines prepared, adopted and published by the Bulgarian Cancer Society for oncological diseases, including rare tumours, clinical guidelines for Gaucher disease, neuromuscular diseases, thalassemia.

Training and education initiatives

The first Eastern Europe Rare Diseases Summer School¹² designed for Russian health authorities and legislative institutions was held on 11-18 September 2011. It was a joint initiative of BAPES, the National Association of Rare Diseases Patient Organisations "Genetics" (Russia) and the Italian National Centre for Rare Diseases (CNMR). The event gave the Russian policy and decision makers an opportunity to learn more about rare disease topics and to understand the significant added-value that rare diseases actions and measures bring to the table. The participants came from a wide range of public fields – federal and regional legislative bodies and health authorities, leading medical institutions, academia, patient organisations and the pharmaceutical industry. The week-long event, which covered a variety of topics including centres of expertise, orphan medicinal products, registries, and national plans, was considered a success by attendees, who reported feeling much better informed on the needs of rare disease patients by the end of the training. Several rare diseases school initiatives are being planned for 2012.

Furthermore, BAPES organised for a second consecutive year in a row a two-day rare disease training seminar for medical students. 30 medical students had the chance to get acknowledged with the main rare diseases concepts, such definition, major problems, important initiatives, etc. The information and education services, offered by ICRDOD and Orphanet were also presented as high quality and reliable source of information, that medical students could use anytime now during their training or further in their future professional practice. Patient representatives took part in the event too, giving personal testimonials and their own point of view on rare diseases issues.

¹⁰ http://raredis.org/pub/OD_Report_04042011_EN.pdf

¹¹ http://www.raredis.org/?page_id=2311&mel=7&smel=71&lang=en

¹² http://raredis.org/pub/Newsletter/Rare_Diseases_Summer_School_2011.pdf

A training workshop for people with rare diseases was held on 1-7 May 2011 in Veliko Tarnovo.

National rare disease events in 2011

Every January, there is an annual meeting of the Consultants of the Information Centre for Rare Diseases and Orphan Drugs (ICRDOD).

For the fourth consecutive year Rare Disease Day was marked in Bulgaria by various events organised by the National Alliance of People with Rare Diseases with the support of BAPES.

This year's event started on 12-13 February 2011 in Plovdiv with a training workshop "Psychological methods – way of self-help to improve quality of life of people with rare diseases and their families". On 28 February 2011 a formal press-conference was held in Sofia. Rare disease stakeholders presented the newest achievements in this field across Europe and current problems in Bulgaria. The main focus of the Rare Disease Day in Bulgaria was the relation between patients and GPs. A series of training workshops on rare diseases for general practitioners was organised in Sofia, Plovdiv, Varna, Stara Zagora and Pleven. Leading medical experts presented the specifics of selected rare diseases as cystic fibrosis, pulmonary hypertension, epidermolysis bullosa, primary immunodeficiencies, thalassemia major, hereditary angioedema, Wilson disease, porphyrias, acromegaly. This initiative was a response to the requests of Bulgarian rare diseases patients at last year's Bulgarian EUROPLAN national conference. Parents of children with rare diseases particularly stressed the importance of GPs' awareness of rare diseases and the need for more efficient communication with them. The importance of Orphanet as an important source of quality information on rare diseases' field was outlined during this training workshops. GPs and even profile specialists were reminded that whenever they have a possible rare disease case they should feel free to seek some expert help and refer to validated information such as that of Orphanet. Medical students and patient associations organised a "teddy bear hospital" in Varna to help children overcome their fear of hospitals and doctors by playing games. The finale of the event was a charity rock concert on the main city square in Pleven (27 February 2011). Information was distributed in Bulgaria's major cities on 28 February.

The Second National Conference for Rare Diseases and Orphan Drugs was held on 9-11 September 2011¹³ in Plovdiv. Topics¹⁴ included epidemiological registries for rare diseases, best practice guidelines for rare diseases management, health policy and legislation, access to orphan medicinal products in Bulgaria, the Bulgarian National Plan for Rare Diseases, European projects and programmes. The forum succeeded in creating a stage for a useful discussion of the current problems of rare diseases patients and medical professionals. A particular focus was the underperforming of the current National programme, which has not come yet to establish a national registry or reference centres. Just two years before the planned end of this plan, Bulgarian rare diseases stakeholders agreed that it is crucial to have a clear declaration of political willingness from the Ministry of Health for the implementation of the National plan, as well as an adequate funding for the foreseen activities, so the plan could reach its initial objectives. All the plan-identified measures should be supported in balanced way.

Hosted rare disease events in 2011

The Bulgarian Association for Promotion of Education and Science launched and organised in 2005, 2006, 2008 and 2009, the annual "Eastern European Conference on Rare Diseases and Orphan Drugs". In 2010 for the very first time the event was hosted and co-organised outside Bulgaria, in Saint Petersburg, Russia, in conjunction with the first All-Russian Conference for Rare Diseases and Rarely Used Medical Technologies. It has proved to be an efficient strategy to foster rare diseases progress in Eastern Europe. In 2011, the sixth edition¹⁵ of this initiative was held and co-organised in Istanbul, Turkey.

This excellent collaboration has been also the driving force behind the first ever in Eastern Europe Rare Diseases Summer School for health authorities and legislative bodies, held in Bulgaria on 11-18 September 2011.

The 4th European Symposium on Rare Anaemias¹⁶, an ENERCA project activity, was hosted in Sofia on 19-20 November 2011. It was jointly organised by the European Network for Rare and Congenital Anaemias (ENERCA), the Thalassaemics' Organisation in Bulgaria, the Thalassaemia International Federation and supported by the Bulgarian Scientific Society of Clinical and Transfusion Haematology. The event aimed to disseminate up-to-date knowledge and increase the public awareness about congenital and rare anaemias. The

¹³ www.conf2011.raredis.org

¹⁴ http://raredis.org/pub/Newsletter/Conference_Book_2011.pdf

¹⁵ <http://www.rare-disease2011.org/index.php>

¹⁶ <http://www.enerca2011.otbulgaria.com/regform/brochure.pdf>

3rd Bulgarian Symposium of thalassaemia patients and professionals was integrated in the framework of the 4th European Symposium on Rare Anaemias. The program included an interactive session with patient panellists and doctors, focusing not only on clinical management but also on prevention and social action for thalassaemia and haemoglobinopathies.

Research activities and E-Rare partnership

National research activities

In Bulgaria, there is no specific call for rare diseases at the national fund for research, although rare disease related projects can apply. The National Plan does not envisage any official policies to stimulate research on rare diseases; it only envisages encouraging partnerships.

Participation in European research projects

Bulgaria participates in European rare disease research projects, including: EUROGLYCANET and TREAT-NMD.

E-Rare

Bulgaria is not currently a partner of E-Rare.

IRDIRC

Bulgarian funding agencies have not yet committed national funding to the IRDiRC.

Orphan medicinal products

ICRDOD issued an updated report in March 2011 reviewing access to medicines for rare diseases in Bulgaria¹⁷. The report contains information on important orphan medicinal products activities and explained how they are set up in Bulgaria in 4 sections: orphan medicinal product designation and marketing authorisation; pricing, inclusion in the Positive Drug List (PDL) and reimbursement; mechanisms for accelerated access to innovative medicines; and conclusions.

Orphan medicinal product committee

There is currently no orphan medicinal products specialised committee in Bulgaria. Orphan medicinal products are subject as are all other medicinal products to the Commissions on the pricing of medicines and on the Positive drug list. In order to optimise these procedures, in 2011 the two commissions were merged into a single one under the Ministry of Health. From 2011, orphan medicinal products reimbursed by the Ministry of Health, the second one by the National Health Insurance Fund (NHIF).

Orphan medicinal product incentives

No specific activity reported.

Orphan medicinal product market availability situation

All orphan medicinal products, authorised under centralised procedure in EU could be available in Bulgaria, after adoption of the new Regulation N° 10/17 November 2011 for the conditions and the order of treatment with medicinal products without marketing authorisation in Bulgaria, as well for the conditions and the order for including, changes, excluding and distribution of medicinal products from the list in article 266A, paragraph 2 from the Law of medicinal products for human medicine, which replaced Regulation N° 2/10 January 2001. The important change, regarding availability of orphan medicinal products in the Regulation N° 10/17 November 2011 is that it arranged the distribution of the drugs, including orphan medicinal products, that have been priced but are not available on the Bulgarian market or such that have not been priced and included in reimbursement list. Article 266A is new and was enforced from 5 August 2011, arranging the use of the medicinal products authorised in the EU countries that are not distributed on the Bulgarian market.

Currently in Bulgaria, 28 orphan medicinal products with EMA market authorisation are priced and included in the Positive Drug List (PDL) and 22 orphan medicinal products (from the 28 in PDL) are reimbursed at 100% (10 under Ordinance 34 and 6 under Ordinance 38) and should be available for the patients with rare diseases.

¹⁷ Orphan drugs in Bulgaria: Periodic review of the access to orphan drugs in Bulgaria:
http://raredis.org/pub/OD_Report_04042011_EN.pdf

The drugs available on the market in 2011 on the PDL and included in Ordinance 34¹⁸ are: Afinitor, Atriance, Evoltra, Glivec, Litak, Nexavar, Nplate, Sprycel, Tasigna and Torisel. The drugs available on the market on the PDL and included in Ordinance 38 are: Exjade, Fabrazyme, Revatio, Revolade, Somavert, TOBI, Tracleer, Ventavis, Zavesca and Cerezyme.

Despite the recent increase of these figures, institutions dealing with planning and funding for treatment and rehabilitation of patients with rare diseases still do not have actual and reliable data on the number and distribution of patients in the country and information on the compliance and effectiveness of this expensive treatment.

Orphan medicinal product pricing policy

There is no specific orphan medicinal product pricing policy and orphan medicinal products are subject to the general conditions as any other medicaments. The negotiation of price and level of reimbursement of orphan medicinal products in Bulgaria is determined by the Ordinance on the conditions, rules and procedures for regulating and registering the prices of medicines, and it is based on reference pricing, using data from Romania, France, Estonia, Greece, Slovakia, Lithuania, Portugal, Spain, Belgium, Czech Republic, Poland, Latvia and Hungary.

Orphan medicinal product reimbursement policy

There is no specific orphan medicinal product reimbursement policy and orphan medicinal products are subject to the general conditions as any other medicaments.

Having been priced, orphan medicinal products can be included in the PDL. The Commission on the PDL examines and decides on applications for inclusion, amendments and/or exclusion of drugs from PDL. PDL groups the drugs into 4 annexes: Annex 1 – drugs for treatment, paid under the Health Insurance Act (HIA); Annex 2 – drugs paid by the budget of the medical-treatment facilities under Art. 5 of the Medical Treatment Facilities Act (MTFA) and by the budget of the hospitals with state and/or municipal stake upon Art. 9 and 10 of MTFA; Annex 3 – drugs for treatment outside the scope of HIA, paid in accordance with Art. 82, par. 1, item 8 of the Law on Health; Annex 4 – drugs for treatment of rare diseases, AIDS and infectious diseases. Until the end of 2010 orphan medicinal products in Bulgaria were included in Annexes 3 and 4. From 2011, in conjunction with the new reimbursement schemes, some of them (for rare non-oncological diseases) were transferred to Annex 1 (of medicinal products for treatment, paid under HIA).

Other initiatives to improve access to orphan medicinal products

Changes to Ordinances 34/ 25 Nov 2005 and 38/ 16 Nov 2004 of the Ministry of Health were enforced at the beginning of 2011. The main aim of those changes is to shorten patients' wait for orphan medicinal products. Most of the procedures will be performed by National Health Insurance Fund, instead of Ministry of Health, and the orphan medicinal products will be bought directly, according to price (the orphan medicinal products with respective lowest price will be reimbursed).

Orphan devices

No information reported.

Specialised social services

Respite care services and therapeutic recreational programmes are provided in certain medical centres in Bulgaria and are partially reimbursed by the National Health Insurance Fund.

In Bulgaria, there are currently no specialised programmes for people for rare diseases: these patients are forced to seek alternatives in the existing general schemes for the rehabilitation and integration of people with disabilities which do not often meet European standards and recommendations in the area. They are unevenly distributed across the country and public awareness of these services is low. In addition, rare disease patients may be denied access as the Territorial Expert Medical Commission's legislation is not adapted to the specificities of rare disease. As such, one of the priorities of the National Plan is to work on an integrative approach and specialised programmes for physical and social rehabilitation of rare disease patients, however no progress has been made to date, and patients feel that specialised services for rare diseases should not be separated or be in opposition to current programmes for people with disabilities.

¹⁸ Information taken from the report *Orphan drugs in Bulgaria: Periodic review of the access to orphan drugs in Bulgaria (March 2011)*: http://raredis.org/pub/OD_Report_04042011_EN.pdf

DEVELOPMENT OF RARE DISEASE ACTIVITIES IN 2011 IN BULGARIA

National plan/strategy for rare diseases and related actions

A National Consulting Council on Rare Diseases has been established by the Ministry of Health, and meets once a month to supervise the progress and implementation of the national plan for rare diseases. Since 2011 there has been a tendency to gradually transfer all rare diseases treatment coverage from the Ministry of Health to National Health Insurance Fund. However, the Ministry of Health stays a major actor in rare diseases treatment provision through the Ministry of Health-operated Fund for Children's Treatment and Commission for Treatment Abroad.

Registries

Following the very successful model of "The National registry of thalassaemia major patients in Bulgaria", BAPES (Bulgarian Association for the Promotion of Education and Science) has initiated recently 5 new rare diseases registries. In May 2011 the first results from a joint study of BAPES and Wilson disease patient association were published¹⁹. The Crohn Disease National Registry is already working and its first statistics²⁰ were officially adopted in June 2011 at a Crohn Disease national workshop. The Bulgarian Scientific Society of Gastroenterology, Gastrointestinal Endoscopy and Abdominal Echography and the university gastroenterology clinics throughout the country have greatly supported and contributed to both Crohn and Wilson patient registries. Just before the Second National Conference for Rare Diseases in September 2011 the provisional results of two new rare diseases patient registries were announced for Gaucher disease and Mucopolysaccharidosis type 2. The corresponding patient associations have provided data, which were analysed by BAPES. In December 2011 BAPES has reached agreements with the Bulgarian Scientific Society for Clinical and Transfusion Haematology and the Bulgarian Scientific Chirurgical Society for launching two new rare diseases registries for primary myelofibrosis and neuroendocrine tumors respectively. A unique character of all BAPES-managed epidemiological registries for rare diseases is that they involve joint activities by all relevant stakeholders.

Sources of information on rare diseases and national help lines

Official information centre for rare diseases

The Information Centre for Rare Diseases and Orphan Drugs (ICRDOD)²¹ site was substantially renewed and upgraded at the end of 2011. Besides a new look and new layout of content, the site offers several new features for its users, such a subscription for its newsletter "Rare Diseases & Orphan Drugs", an online registry of rare diseases patients, an updated Rare Diseases Library in Bulgarian, as well as better interaction between the different users and ICRDOD team.

ICRDOD published in March 2011 an updated review of the access to orphan medicinal products for rare diseases in Bulgaria²²: the report contains 4 sections: orphan medicinal product designation and marketing authorisation; pricing, inclusion in the Positive drug list and reimbursement; mechanisms for accelerated access to innovative medicines; conclusions. There are 2 annexes, attached to the review: list of orphan medicinal products in EU and Bulgaria, which contains information about the trade name, ATC code, active substance, indication(s), marketing authorisation holder and date of marketing authorisation for each item (additionally, it is indicated whether the drug is present in the Positive drug list of Bulgaria and if it is reimbursed by public funds); and a list of references.

Training and education initiatives

The first Eastern Europe Rare Diseases Summer School²³ designed for Russian health authorities and legislative institutions was held on 11-18 September 2011. It was a joint initiative of BAPES, the National Association of Rare Diseases Patient Organisations "Genetics" (Russia) and the Italian National Centre for Rare Diseases (CNMR). The event gave the Russian policy and decision makers an opportunity to learn more about rare

¹⁹ http://www.raredis.org/?page_id=2447&mel=4&smel=44&lang=en

²⁰ http://www.raredis.org/?page_id=2454&mel=4&smel=43&lang=en

²¹ <http://www.raredis.org/>

²² http://raredis.org/pub/OD_Report_04042011_EN.pdf

²³ http://raredis.org/pub/Newsletter/Rare_Diseases_Summer_School_2011.pdf

disease topics and to understand the significant added-value that rare diseases actions and measures bring to the table. The participants came from a wide range of public fields – federal and regional legislative bodies and health authorities, leading medical institutions, academia, patient organisations and the pharmaceutical industry. The week-long event, which covered a variety of topics including centres of expertise, orphan medicinal products, registries, and national plans, was considered a success by attendees, who reported feeling much better informed on the needs of rare disease patients by the end of the training. Several rare diseases school initiatives are being planned for 2012.

Furthermore, BAPES organised for a second consecutive year in a row a two-day rare disease training seminar for medical students. 30 medical students had the chance to get acknowledged with the main rare diseases concepts, such definition, major problems, important initiatives, etc. The information and education services, offered by ICRDOD and Orphanet were also presented as high quality and reliable source of information, that medical students could use anytime now during their training or further in their future professional practice. Patient representatives took part in the event too, giving personal testimonials and their own point of view on rare diseases issues.

A training workshop for people with rare diseases was held on 1-7 May 2011 in Veliko Tarnovo.

National rare disease events in 2011

Every January, there is an annual meeting of the Consultants of the Information Centre for Rare Diseases and Orphan Drugs (ICRDOD).

For the fourth consecutive year Rare Disease Day was marked in Bulgaria by various events organised by the National Alliance of People with Rare Diseases with the support of BAPES.

This year's event started on 12-13 February 2011 in Plovdiv with a training workshop “Psychological methods – way of self-help to improve quality of life of people with rare diseases and their families”. On 28 February 2011 a formal press-conference was held in Sofia. Rare disease stakeholders presented the newest achievements in this field across Europe and current problems in Bulgaria. The main focus of the Rare Disease Day in Bulgaria was the relation between patients and GPs. A series of training workshops on rare diseases for general practitioners was organised in Sofia, Plovdiv, Varna, Stara Zagora and Pleven. Leading medical experts presented the specifics of selected rare diseases as cystic fibrosis, pulmonary hypertension, epidermolysis bullosa, primary immunodeficiencies, thalassemia major, hereditary angioedema, Wilson disease, porphyrias, acromegaly. This initiative was a response to the requests of Bulgarian rare diseases patients at last year's Bulgarian EUROPLAN national conference. Parents of children with rare diseases particularly stressed the importance of GPs' awareness of rare diseases and the need for more efficient communication with them. The importance of Orphanet as an important source of quality information on rare diseases' field was outlined during this training workshops. GPs and even profile specialists were reminded that whenever they have a possible rare disease case they should feel free to seek some expert help and refer to validated information such as that of Orphanet. Medical students and patient associations organised a “teddy bear hospital” in Varna to help children overcome their fear of hospitals and doctors by playing games. The finale of the event was a charity rock concert on the main city square in Pleven (27 February 2011). Information was distributed in Bulgaria's major cities on 28 February.

The Second National Conference for Rare Diseases and Orphan Drugs was held on 9-11 September 2011²⁴ in Plovdiv. Topics²⁵ included epidemiological registries for rare diseases, best practice guidelines for rare diseases management, health policy and legislation, access to orphan medicinal products in Bulgaria, the Bulgarian National Plan for Rare Diseases, European projects and programmes. The forum succeeded in creating a stage for a useful discussion of the current problems of rare diseases patients and medical professionals. A particular focus was the underperforming of the current National programme, which has not come yet to establish a national registry or reference centres. Just two years before the planned end of this plan, Bulgarian rare diseases stakeholders agreed that it is crucial to have a clear declaration of political willingness from the Ministry of Health for the implementation of the National plan, as well as an adequate funding for the foreseen activities, so the plan could reach its initial objectives. All the plan-identified measures should be supported in balanced way.

Research activities and E-Rare partnership

IRDIRC

Bulgarian funding agencies are not yet committed members of the IRDiRC.

²⁴ www.conf2011.raredis.org

²⁵ http://raredis.org/pub/Newsletter/Conference_Book_2011.pdf

Orphan medicinal products

ICRDOD issued an updated report in March 2011 reviewing access to medicines for rare diseases in Bulgaria²⁶. The report contains information on important orphan medicinal products' activities and explained how they are set up in Bulgaria in 4 sections: orphan medicinal product designation and marketing authorisation; pricing, inclusion in the Positive Drug List (PDL) and reimbursement; mechanisms for accelerated access to innovative medicines; and conclusions.

Orphan medicinal product committee

Orphan medicinal products are subject as are all other medicinal products to the Commissions on the pricing of medicines and on the Positive drug list. In order to optimise these procedures, in 2011 the two commissions were merged into a single one under the Ministry of Health. From 2011, orphan medicinal products reimbursed by the Ministry of Health, the second one by the National Health Insurance Fund (NHIF).

Orphan medicinal product market availability situation

All orphan medicinal products, authorised under centralised procedure in EU could be available in Bulgaria, after adoption of the new Regulation N° 10/17 November 2011 for the conditions and the order of treatment with medicinal products without marketing authorisation in Bulgaria, as well for the conditions and the order for including, changes, excluding and distribution of medicinal products from the list in article 266A, paragraph 2 from the Law of medicinal products for human medicine, which replaced Regulation N° 2/10 January 2001. The important change, regarding availability of orphan medicinal products in the Regulation N° 10/17 November 2011 is that it arranged the distribution of the drugs, including orphan medicinal products, that have been priced but are not available on the Bulgarian market or such that have not been priced and included in reimbursement list. Article 266A is new and was enforced from 5 August 2011, arranging the use of the medicinal products authorised in the EU countries that are not distributed on the Bulgarian market.

Despite the recent increase of these figures, institutions dealing with planning and funding for treatment and rehabilitation of patients with rare diseases still do not have actual and reliable data on the number and distribution of patients in the country and information on the compliance and effectiveness of this expensive treatment.

²⁶ Orphan drugs in Bulgaria: Periodic review of the access to orphan drugs in Bulgaria:
http://raredis.org/pub/OD_Report_04042011_EN.pdf

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²⁷ 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.

²⁸ All websites and documents were last accessed in May 2012. A more detailed list of sources is available in the full report:
<http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArtRDActivities.pdf>