www.raredis.org June 2013 (Issue 16, Year IV)

RARE DISEASES ORPHAN DRUGS

Official Newsletter of the Bulgarian Association for Promotion of Education and Science (BAPES)

Dear friends,

FOCUS ON:

LET'S ADD LIFE!

Rare diseases topics are once again in the headlines. The Bulgarian Cystic Fibrosis Patient Association has been fighting for years for the adoption and implementation in Bulgaria of the so called European consensus standard for treatment of this rare disease. Cystic fibrosis is actually the genetic disease with highest number of carriers among Caucasians. It is a very illustrative fact that a measure, which is predominantly organisational and even budget saving, but most importantly it is rescuing human lives, has been ignored for a long time and gathering dust at different levels of the administration. At the same time, patients with cystic fibrosis are left on their own with multiple life-threatening complications and facing no understanding of this basic problem – the lack of an adequate framework for treatment of cystic fibrosis in Bulgaria. Statistics are miserable. While in the countries where the above mentioned standard is applied, quality and expectancy of life of cystic fibrosis patients steadily increased, in Bulgaria these indicators are far behind. It is very said but the lack of public interest and awareness of rare diseases is the biggest problem for people with rare diseases in Bulgaria, their families and medical professionals.

Earlier this year, Cystic Fibrosis Association took a new approach against the refusal of the system to hear their voice. Patients and their relatives waged a campaign called "Cystic Fibrosis – Let's Add Life". It does not focus on workshops and expert groups, it tends to show ordinary patients and their families, their constant worries and concerns, their hopes that they would fight the disease despite all obstacles and barriers. Whether there will be a happy ending for the people with cystic fibrosis in Bulgaria, it is yet to be known. But we must admit their bravery and courage to take their fate into their own hands and not to leave it to the general apathy and indifference.

Finally, we want to use the opportunity to invite you to the 4th National Conference for Rare Diseases and Orphan Drugs. This year's event special guest speaker will be Dr. Ben Carson, world-renowned Professor of neurosurgery, plastic surgery, oncology and pediatrics, and Director of pediatric surgery at Johns Hopkins Hospital in Baltimore, Maryland. Take part in the biggest forum for rare diseases and support the cause of rare diseases.

HAVE NICE MINUTES WITH "RARE DISEASES & ORPHAN DRUGS"!

4-th NATIONAL CONFERENCE
FOR RARE DISEASES AND ORPHAN DRUGS

13-14 September 2013
Congress Centre of Novotel-Plovdiv

- **Guest speaker – Dr. Ben Carson, Professor of neurosurgery, plastic surgery, oncology and pediatrics, Johns Hopkins Hospital, Baltimore (Maryland)**
- **Themes: European Directive on patients' rights in cross-border health care, Access of patients with rare diseases to diagnosis and treatment, Centres of expertise and reference networks for rare diseases, Health technology assessment for rare diseases**
- **Poster session and print collection of conference presentations and posters**

More information and early registration on:

www.conf2013.raredis.org

CYSTIC FIBROSIS PATIENTS AND PARENTS STAND FOR THE ADOPTION AND IMPLEMENTATION OF A TREATMENT STANDARD

"Cystic Fibrosis – Let's Add Life" Campaign is gaining momentum through various events, meetings and charities

Since three years we have been holding discussions with representatives of the Ministry of Health that the adoption of a cystic fibrosis treatment standard based on the current European consensus will finally allow a multidisciplinary approach in the follow up of patients and will help establishing a National Centre for Cystic Fibrosis. These combined measures would prolong survival 2, even 3 times. We have just got to the Minister of Health – and now there is a threat to get back to the starting point and then again to go explaining what the disease means, what specific treatment, cares and environment it requires. This is what Svetlana Atanasova, chairwoman of Cystic Fibrosis Association, has been telling the media since February. It is very stressful now, that with all the changes in the country, our problems may be left aside again, she said at a press conference in Plovdiv in February, when "Cystic Fibrosis – Let's Add Life" campaign was launched. At particular moment Bulgaria was shaken by protests and the government resigned.

About a week later, on 21 February, a 12 year old child suffering from cystic fibrosis was gone. Teddy from the small town of Provadia was supposed to go for a treatment in Switzerland, which was planned for March in order to get stabilised and eventually be included in a waiting list for lung transplantation. Many people from across the country had contributed to a fund-raising campaign for the treatment of this boy. Unfortunately, he was just another cystic fibrosis patient that passes away in expectation and hope that the health authorities would take measures to solve these problems. These people, however, can not get out to a mass protest. They live with the feeling that their voice for equal access to adequate treatment would never be heard.

On February 14, on a meeting at the Ministry of Health with medical professionals it was decided to establish a working group to transfer and implement the much needed European consensus standard for the cystic fibrosis treatment. There is no evidence, however, that the cabinet has yet to officialise the work on this task force, Svetlana Atanasova says.

All these issues, together with the personal stories of patients with cystic fibrosis and their families has became the focus of a meeting with the candidates for the Bulgarian legislative elections in early May. During this specific occasion forum, F2F TV journalist Ekaterina Kostova tried to show the public whether a cause related to human health, may bring together policy makers particularly during the period of election campaign when anyone is ready to promise anything. 7 of the 17 invited parties and coalitions responded to the call to hear the voice of people with rare diseases. Now, when 3 of these parties are already in Parliament, patients and parents will insist legislators to do their job because of the public commitment they made not to sink cystic fibrosis problem down into the total disorder of the health system.

For the family of Pavlina and Dragomir Sivakovi these problems mean daily struggle. Not only because their 4 years old son Toshko suffers from cystic fibrosis, but also because of the inadequate treatment that the health system is offering to these children. Until he becomes 6, he can not use inhaled antibiotic by the National Health Insurance Fund. That means that bacteria would be “eating” away of his lungs for two more years, his father adds. All parents are in similar situation. Because of the inadequate treatment, life expectancy for cystic fibrosis in Bulgaria is about 12.5 years, while in Europe it is almost 50.

I'm tired of being positive. Every day is a similar type of struggle and nothing depends on me. It is the health system that takes the decision and does not allow me to change my medications, even if they are no longer efficient. I feel doomed, 29-year Boryana Lazova of Pazardzhik tells. Over the past two months she got a serious infection and urgently needed to be hospitalised. Her friends launched a campaign to collect funds for the expensive antibiotics and vitamins that she needs to take. She was firstly helped by Kamelia Atanasova, another cystic fibrosis patient, who gave her own medication.

And if there is no one to help gathering funds for expensive drugs in such an emergency? What happens, patients and families ask.

Cystic Fibrosis Association explains that the problem is that there is separate clinical pathway for cystic fibrosis and these patients are treated within the bronchopneumonia pathway. There is a penultimate resolution of the court on this case. Ministry of Health has allowed discrimination against patients with cystic fibrosis, as there is no independent clinical pathway for the treatment of this disease. That is the decision of the Sofia Administrative Court from March. It confirms a previous decision by the Commission for protection against discrimination. But the Ministry of Health is currently appealing it. What will decide the Supreme Administrative Court? This is the question that people affected by cystic fibrosis expect with a sinking heart. Every day means life for these patients.

Searching for institutional and public support, the “Cystic Fibrosis – Let’s Add Life” campaign created a Facebook page that tells stories of people suffering from the disease, as well as presents initiatives, helping the cause for the introduction of the so called European standard of treatment. It also organised a journalistic competition to persuade media to put the focus of attention on this subject, which is vital for many Bulgarian families. The good news is that more and more people are taking part in this campaign, as dozens of media are becoming aware of the cystic fibrosis treatment problems. It turns out that people want to help and contribute to the extent possible.

A charity sale of handmade cards in Total Sports Club collected 107.40 Levs that were used were for buying oxygen concentrators, without which in emergencies people with cystic fibrosis can not breathe. Another sale of charity cards donated funds for the treatment of Boryana Lazova. 1779.10 Levs for oxygen concentrators were gathered from three more charities: June 1st kids workshop, charity event “Sissy” in Kocho Chestimenski School, and rock concert of RENEGADE and IVORY TWILIGHT groups at the Plovdiv Theatre.

Within the "Cystic Fibrosis – Let's Add Life" campaign, two patient rooms and a medical office for cystic fibrosis were renovated and quipped at the University Hospital "St. George" by donations. Svetlana Atanasova says that means a lot for the cystic fibrosis patients, because high hygiene standards and separate rooms help avoiding cross contamination. It shortens the period of treatment and improves therapy quality. Plovdiv Metropolitan Bishopship donated icons of the Virgin Mary to protect cystic fibrosis patients. In August Plovdiv Metropolitan Bishop Nikolay will personally support the campaign.

Sustainable solution of the problem of access to quality treatment follow-up of people suffering from cystic fibrosis, however, can only happen with the support of politicians. Therefore "Cystic Fibrosis – Let's Add Life" campaign continues to seek wider and wider support. The Ombudsman of Bulgaria Konstantin Penchev has already stood beside the patients with cystic fibrosis and their legitimate quest.

The solution is not just about money, on the contrary – it can even save money. The legislative framework needs to be changed to provide a new approach to rare diseases, Vladimir Tomov, chairman of the National Alliance of People with Rare Diseases says. The Ombudsman assured that he will not only help Cystic Fibrosis Association meet the Minister of Health Dr. Tanya Andreeva, but he is also committed to implementation of the European consensus standard, as he has already supported other patient with rare diseases to solve their problems. He received the proposed changes that would help patients with cystic fibrosis get a chance to access quality treatment and have a better life. The Proposals were also sent to the new Minister of Health along with a request for a meeting.

And while people with rare diseases are waiting for their health and life to be finally put on the agenda of the Bulgarian politicians and lawmakers, the World Organization for Cystic Fibrosis is ready to help the Bulgarians cystic fibrosis patients and donate about $ 1 million for the creation of National Centre for Cystic Fibrosis. These funds are not in cash, but rather in medication, supplies, training of medical staff for one year, but if only the government ensures that it will continue supporting the Centre after that.

Now, it is health authorities' and politicians' turn. They must finally hear the voice of people with cystic fibrosis. And to do their job, so that access to quality healthcare in our country is guaranteed for everyone. "Cystic Fibrosis – Let's Add Life" campaign will continue until that happens... You can start supporting by the liking its Facebook page.

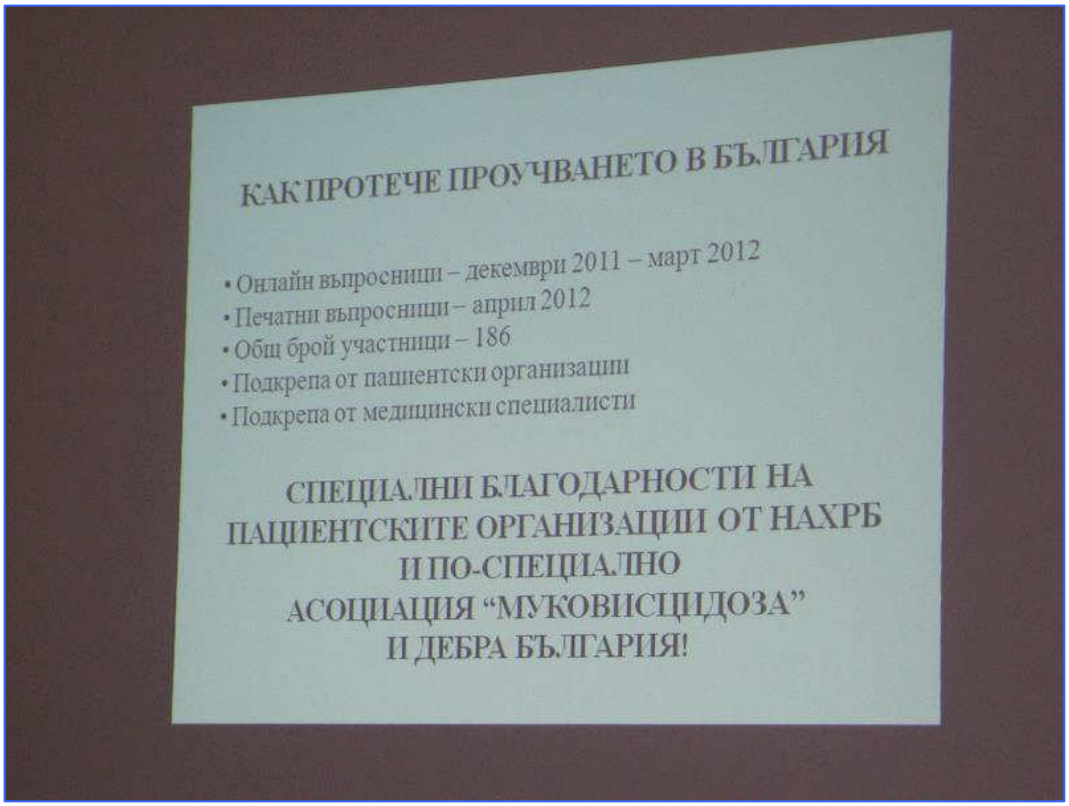
Text and pictures are part of the *"Cystic Fibrosis – Let's Add Life"*, campaign of Cystic Fibrosis Association to adopt the European consensus standard for the treatment of this disease in Bulgaria. Special thanks to Ms. Svetlana Atanasova, chairwoman of Cystic Fibrosis Association and to the journalist Ms. Ekaterina Kostova.

Facebook page of the campaign – http://www.facebook.com/pages/Муковисцидоза-да-добавим-живот/141042389396131

SUCCESSFUL END OF BURQOL-RD PROJECT

The largest ever European study on socio-economic burden and quality of life in patients with rare diseases and their families was completed in May

Because of their characteristics, rare diseases require the combined efforts of medical, health and social care professionals, policy makers, researchers in order to create and improve the existing conditions for treatment and follow-up, resulting in increased life expectancy and improved health-related quality of life. Appropriate and justified assessment of indicators such as socio-economic burden and quality of life of people with rare diseases and their families is essential for the preparation, adoption and implementation of EU and national policies in this field.



At the end of May 2013 the largest ever survey of patients with rare diseases in Europe was completed, as part of the European project BURQOL-RD. This three-year project is co-funded by the European Commission and aims to generate a specific model for assessing socio-economic burden and health-related quality of life in patients with rare diseases and their carers. A pilot study was conducted to verify in practice the tools for gathering this information, as well as the methodology for measuring these two indicators for rare diseases.

After detailed research, analysis and several round of consultation, 10 specific rare diseases were defined to be studied within the BURQOL-RD project. This set was required to be heterogeneous enough in terms of clinical characteristics, treatment options, prevalence, ect. So, the final data obtained could be representative for all over 7 000 different rare diseases. The study itself focused on cystic fibrosis, Prader-Willi syndrome, hemophilia, Duchenne muscular dystrophy, fragile X chromosome syndrome, epidermolysis bullosa, scleroderma, mucopolysaccharidosis, juvenile idiopathic arthritis and histiocytosis X.

The pilot study was held in 8 European countries (Spain, Bulgaria, Hungary, Germany, Italy, Sweden, France and the United Kingdom). Bulgarian patients and their carers could take part from December 2011 to April 2012 through online survey forms and printed questionnaires. 188 responses were received. The information collected included a socio-demographic profile, self reported assessment of health-related quality of life (EQ-5D, Barthel index, etc.), satisfaction with the health system, analysis of direct (medical, formal and non-medical) and indirect costs for each of 10 specific rare diseases.

COUNTRY	RESPONSES
Spain	794
Bulgaria	188
Germany	612
Italy	1039
Hungary	420
United Kingdom	372
Sweden	226
France	1134

The methodological framework to measure the socio-economic burden and health-related quality of life in rare diseases, which will be based on the results of the 8 European survey studies, will be of great importance for both health authorities and patients. It will allow rapid transfer of best practices, consistency and comparability of availability and access to health resources for rare diseases in each of the Member States of the EU. It would also explore the relationship between health-related quality of life and access to healthcare services. The full report on the project, including an analysis of the health and social services received by people with rare diseases in the EU, information on the current socio-economic burden and health-related quality of life, as well as details of the elaborated tools for assessment and monitoring of rare diseases in the EU, will be ready be ready and presented by October 2013.

BURQOL-RD coordination team and Information Centre for Rare Diseases and Orphan Drugs would like to express special thanks gratitude to the following patient organisations and medical professionals (in alphabetical order), who have contributed to the study in Bulgaria: National Alliance of People with Rare Diseases, Cystic Fibrosis Association, Bulgarian Association of Hemophilia, DEBRA Bulgaria, Bulgarian Association Prader-Willi Syndrome, National Association Mucopolysaccharidosis, Assoc. Prof. Alexey Savov (National Genetic Laboratory, Sofia), Dr. Veselina Goranova (University Hospital "St. George", Plovdiv), Assoc. Prof. Violeta Yotova (University Hospital "St. Marina", Varna), Dr. Denka Stoyanova (Pediatric Oncohematology Hospital, Sofia), Dr. Dimitrina Konstantinova (University Hospital "St. Marina", Varna), Assoc. Prof. Iva Stoeva (University Pediatric Hospital, Sofia), Ms. Ivelina Alexandrova (Logopedia.bg), Assoc. Prof. Ivelina Yordanova (University Hospital "Prof. Stranski", Pleven), Assoc. Prof. Katia Kovacheva (University Hospital "Prof. Stranski" Pleven), Dr. Katia Sapunarova (University Hospital "St. George", Plovdiv), Dr. Lilia Ivanova (University Hospital "St. George", Plovdiv), Dr. Liliana Grozdanova (University Hospital "St. George", Plovdiv), Assoc. Prof. Maria Simeonova (University Hospital "Prof. Stranski", Pleven) , Assoc. Prof. Maria Spasova (University Hospital "St. George", Plovdiv), Assoc. Prof. Radka Tincheva (University Pediatric Hospital, Sofia).

HEREDITARY SPASTIC PARAPLEGIA

Definition and prevalence

Hereditary spastic paraplegia (HSP), also called familial spastic paraplegia or Strümpell-Lorrain disease, is a genetically and clinically heterogeneous group of inherited neurodegenerative disorders, characterised primarily by progressive spasticity and hyperreflexia in lower limbs as a result of nerve damage. NSP affects approximately 1 in 20 000 individuals, regardless of gender. In clinical aspect, NSP can be divided into pure and complex forms. The first are defined by slowly progressive weakness, spasticity in lower limbs, and occasional hypertonic urinary disturbances and reduction of lower extremity vibration sense. Complex forms feature additional neurological and non-neurological damages.

Etiology

Etiology and pathogenesis of this disease are not fully understood yet. Patoanatomy shows degeneration of the ends of the corticospinal tracts within the spinal cord. The ends of the longest fibers, which supply the lower extremities, are affected to a much greater extent than the fibers to the upper body. The disease is inherited as an autosomal dominant (over 70% of cases), autosomal recessive or X-linked recessive trait, and multiple recessive and dominant forms exist. Currently, over 40 genetic loci associated with various forms of HSP have been defined. However, only eleven autosomal and two X-linked genes have been identified to date, the genetic basis for most forms is to be further studied.

Diagnosis

The initial diagnosis is based on family history and clinical examination. Physical examination shows decreased sensitivity in the distal parts of limbs, hyperactive reflexes, and increased muscle tone. In general, the peripheral nerves are not affected in patients with pure forms of the disease, but there are reported rare cases of reduced perception of acute stimuli in below knees. Deep tendon reflexes are pathologically increased in lower extremities. Further examination is required (image diagnosis, electroencephalography, long chain fatty acids, electromyography, and human T-cell lymphotropic virus type 1 serology), so differential diagnosis could exclude other syndromes. For example, MRI is an important procedure for the exclusion of other common neurological diseases, such as multiple sclerosis, but also for detection of concomitant disorders. Final confirmation of diagnosis can be provided by genetic tests for HSP identified genetic mutations.

Clinical picture

The main symptom is progressive, often severe spasticity of lower extremities. In uncomplicated autosomal dominant HSP after normal gestation, delivery, and early childhood development, subjects develop leg stiffness and gait disturbance (eg., stumbling, tripping) because of difficulty in dorsiflexing the foot and weakness in hip flexion. Classic symptom of HSP is progressive difficulty in walking, but severity varies. Some patients eventually may require the use of a wheelchair, while others may never need any type of assistive device. Other features of the disease include:

- decreased sense of balance;
- urinary problems;
- visual disturbance;
- fasciculations;
- dementia and seizures;
- peripheral neuropathy, cerebellar ataxia, and sensory disturbances.

Listed symptoms are not mandatory and may not be developed in all patients. Neurologic examination reveals no evidence of reduced mentation and cranial nerve dysfunction.

Treatment

Currently, no specific treatment exists to prevent, retard, or reverse the progressive disability in patients with HSP. Therapies mainly consist of symptomatic medical management and promotion of physical and emotional well-being. Medicinal therapies include muscle relaxants and spasmolytic agents. Botulinum toxin may be applied to reduce muscle overactivity. Antidepressants are used in patients, experiencing clinical depression. Orthoses may be required in case of footdrop. Surgical treatment targets frequent contractures and tendon problems.

Although it is a progressive disorder, the prognosis for people with NSP varies considerably. The disease primarily affects lower limbs, although upperbody may be damaged in some individuals too. There are reported cases of serious disability, as well as cases that are fully compatible with a productive and fulfilling life. The majority of patients with HSP have a normal life expectancy.

Rehabilitation and follow-up cares

Regular physical therapy is important to maintain and improve range of motion and muscle strength. Although it does not reduce the degenerative process within the spinal cord, individuals with HSP must maintain an exercise regimen at least several times each week, guided by their physical therapist. Exercise can help retain or improve muscle strength, minimize atrophy of the muscles caused by disuse, increase endurance and reduce fatigue, help prevent spasms and cramps.

Physiotherapy is aimed at maintaining the overall functional status, as well as managing accompanying symptoms of the disease such as pain, stiffness, poor coordination and motor difficulties. Physical rehabilitation uses 3 complementary approaches towards NPS. These are manual therapy, exercises and electrotherapy. They adjust and strengthen muscles and joints, increasing overall operational capacity of the body.

Last but not least, this rehabilitation complex has a positive psychological effect on the patient, and acts as a functional readjustment instrument. Physiotherapy promotes the ability to independently perform daily activities.

Bibliography

1. Tallaksen CME, Dürr A, Brice A. Recent advances in hereditary spastic paraplegia. Current Opinion in Neurology, 2001, 14(4): 457-463.
2. Fink JK. Hereditary spastic paraplegia. Current Neurology and Neuroscience Reports, 2006, 6(1):65-76.
3. McDermott CJ, White K, Bushby K et al. Hereditary spastic paraparesis: a review of new developments. J Neurol Neurosurg Psychiatry 2000;69:150-160
4. Erichsen AK, Koht J, Stray-Pedersen A et al. Prevalence of hereditary ataxia and spastic paraplegia in southeast Norway: a population-based study. Brain: a journal of neurology, 2009, 132(6): 1577–88.
5. Schüle R, Schöls L. Genetics of hereditary spastic paraplegias. Semin Neurol. 2011, 31(5):484-93.
6. Fourtassi M, Jacquin-Courtois S, Scheiber-Nogueira MC et al. Bladder dysfunction in hereditary spastic paraplegia: a clinical and urodynamic evaluation. Spinal Cord. 2012 Jul;50(7):558-62.
7. Geva-Dayan K, Domenievitz D, Zahalka R et al. Botulinum toxin injections for pediatric patients with hereditary spastic paraparesis. J Child Neurol. 2010 Aug;25(8):969-75.
8. Richardson D, Thompson AJ. Management of spasticity in hereditary spastic paraplegia. Physiother Res Int. 1999;4(1):68-76.

UPCOMING RARE DISEASES CONFERENCES, WORKSHOPS AND INITIATIVES

- **17-21 July – 8th International Prader-Willi Syndrome Conference, Cambridge**
- **3-6 September – International Congress of Inborn Errors of Metabolism, Barcelona**
- **13-14 September – 4th National Conference for Rare Diseases and Orphan Drugs, Plovdiv**
- **19-23 October – Thalassemia International Federation World Congress, Abu Dhabi**
- **1-3 November – 8th ICORD International Conference for Rare Diseases, Saint Petersburg**
- **14 November – World Orphan Drug Congress, Geneva**

ICORD
International Conference on Rare Diseases & Orphan Drugs

Национален Алианс на Хора с Редки Болести

PSYCHOLOGICAL METHODS – HELPING TO IMPROVE QUALITY OF LIFE OF PEOPLE WITH RARE DISEASES AND THEIR FAMILIES

The National Alliance of People with Rare Diseases is organizing a seminar for psychological support for patients with rare diseases and their families. The event will take place on 27-28 July 2013 at Rusalka Hotel in Plovdiv. Psychologists Madlen Algafari, Kalina Miteva and Tsenka Mestanska will share their tips for managing the psychological side of the rare conditions, strengthening mind and personal development.

For further please visit the National Alliance of People with Rare Diseases' official website – http://rare-bg.com/?p=867

Editorial Box

This newsletter is prepared and published by the Bulgarian Association for Promotion of Education and Science (BAPES). The Information Centre for Rare Diseases and Orphan Drugs (ICRDOD) and Medical Centre "RareDis" are projects of BAPES (www.raredis.org).

Postal address:
BG-4017 Plovdiv, 4 Bratya Sveshtarovi Street
e-mail: info@raredis.org || phone/fax: (+ 359 32) 575797

ISSN 1314-359X

The information in this newsletter is provided free for educational purposes and should not be used for self-diagnosis or self-treatment. In case of a health problem you should contact a medical professional!

Editorial staff:

Editor-in-chief: Rumen Stefanov (*stefanov@raredis.org*)
Issue editor: Georgi Iskrov (*iskrov@raredis.org*)
Rare diseases library: Radostina Simeonova *(simeonova@raredis.org)*
Technical secretary: Desislava Dimitrova (*dimitrova@raredis.org*)

For more information: *www.raredis.org*