Recommendations and Proposed Measures for a Belgian Plan for Rare Diseases

An outline of integrated and comprehensive health and social policy actions for patients with a rare disease

Final report

Fund Rare Diseases and Orphan Drugs

managed by the King Baudouin Foundation

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COLOPHON

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Recommendations and Proposed Measures for a Belgian Plan for Rare Diseases. Final Report

An outline of integrated and comprehensive health and social policy actions for patients with a rare disease

The recommendations and proposed measures for a Belgian Plan for Rare Diseases were developed by the Fund for Rare Diseases and Orphan Drugs, managed by the King Baudouin Foundation, and commissioned by the Minister of Social Affairs and Public Health and the Belgian National Institute for Health and Disability Insurance (RIZIV/INAMI).

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PREFACE

Since a number of years, rare diseases are high on the priority list of Europe and Belgium. Rightly so. Most often, rare diseases are chronic, life threatening or strongly debilitating diseases which demand a specific approach and management.
A rare disease affects only few people – less than 5 in 10.000. But because there are 6.000 to 8.000 different rare diseases, the total number of affected patients can be significant. Only in Belgium, it is estimated that 60.000 to 100.000 patients need adapted care and management due to the rareness of their disease.
The care for patients with a rare disease is not yet optimal: sometimes the patient does not get a proper diagnosis or the diagnosis comes late, for others an adapted treatment is not always available or is not known. Also the development of specific drugs for patients with a rare disease is difficult and their dissemination not always optimal.
Nevertheless, in recent years, the perspectives towards a better life, with a higher quality, have increased for patients with a rare disease, both in Belgium, as well as in the rest of the European Union.

Since 2009, the Fund for Rare Diseases and Orphan Drugs, managed by the King Baudouin Foundation, is supported by the Minister of Social Affairs and Public Health to develop a number of recommendations and proposals for measures for a Belgian Plan for Rare Diseases through a contract with the Belgian National Institute for Health and Disability Insurance (RIZIV/INAMI). The Fund got the specific assignment to propose concrete recommendations and measures for a policy plan concerning rare diseases.[1]

This report is the result of a two year multistakeholder deliberation consisting of a broad collaboration with many actors involved in the field of rare diseases. They were organized in 8 thematic working parties and supervised by the Management Committee of the Fund for Rare Diseases and Orphan Drugs.[2] Together, they participated in the elaboration of 42 concrete recommendations and proposed measures within 11 action domains. These domains are:

- Improving the quality of diagnosis, therapy and patient management by setting up expert centres and expert networks
- Codifying and inventorying rare diseases
- Information and communication
- Patient empowerment
- Training and education of health professionals
- Improving access to and financing of diagnosis
- Improving access to and financing of treatment

1 *An interim report was handed to the Minister in May 2010 and can be consulted online: http://www.kbs-frb.be/publication.aspx?id=271066&LangType=1033*

2 *A complete composition of the working groups and the Management Committee is given in addenda 9 and 10.*

- Comprehensive care for the patient
- Promoting research and transfer of research to diagnostics and treatment
- Management of the future Belgian Plan for Rare Diseases
- Ethics and governance

The report which is presented here was approved by the Management Committee of the Fund for Rare Diseases and Orphan Drugs on May 10, 2011. The statements in this report do not necessarily represent the individual views of the members of the Management Committee, neither of the organizations they represent or in which they take part.

The Fund hopes that its work, of which the results are presented in this document, will contribute to a solid Belgian Plan for Rare Diseases with a thought-out range of global and integrated actions in the healthcare management and the social policy for patients with a rare disease.

This report was handed over to the Minister of Social Affairs and Public Health, Ms. Laurette Onkelinx, at the beginning of October; it does not necessarily reflect the position and/or point of view of the Minister.

CONTENT

EXECUTIVE SUMMARY

The specific problems and needs of patients with rare diseases have been reported and explained in several important European documents, such as the 'Communication from the Commission on Rare Diseases: Europe's Challenges', published on 11 November 2008, and the 'Council Recommendation' of 8 June 2009 on 'An action in the field of rare diseases'.
Both the Commission Communication and Council Recommendation indicate that dedicated National Plans or Strategies, pursuing a comprehensive and integrated approach to the delivery of health and social care for rare disease patients are necessary to actually improve the condition of these patients.

The Fund for Rare Diseases and Orphan Drugs, managed by the King Baudouin Foundation, was contracted by Ms. Laurette Onkelinx, Belgian Minister of Social Affairs and Health, to delineate recommendations and proposals for measures which could form the basis of a Belgian Plan for Rare Diseases. These proposals are described in the 'Recommendations and proposed measures for a Belgian Plan for Rare Diseases'.

An effective and comprehensive strategy for rare diseases at national and regional level, within the context of European collaboration, provides immense new opportunities: it will not only improve the quality of services, health outcomes, quality of life and social rehabilitation of people affected by rare diseases and of their families, it can also assure a more efficient use of public resources devoted to health and social care. Without doubt, such a strategy, under the form of a Belgian Plan for Rare Diseases, will require new investments. On the other hand, these investments will be compensated by savings on inadequate medical services, by better health and quality of life of many thousands of Belgian citizens, who will increase their chances to participate in society.

The 42 recommendations and proposed measures in the 'Recommendations and proposed measures for a Belgian Plan for Rare Diseases' have the aim, by 2016, to diagnose and to treat, in multidisciplinary expert settings, approximately 18.000 patients with a rare disease, in surplus of the current situation. These recommendations and proposals for measures will generate an extra cost for the health care budget, in addition to the efforts already being made today. The additional effort for these proposed measures is estimated to be 34,8 million Euro per year for the period 2012-2016. This means a total of 174 million Euro for the whole period of five years. Of the 42 proposed measures, two generate 68% of this cost. The recommendations foresee a gradual implementation over time of these two measures, making it possible to prevent a possible derailment of the budget.

The costs for these proposals can be divided between:

- an investment cost of 17 million Euro over the 5 years of the duration of the Belgian Plan. More than half of this budget will be invested in research programs;
- yearly recurrent costs need in largest part being taken up by the budget of the health insurance. These costs can incur to 45 million Euro during the last year of the Plan.

Certain proposed costs cannot be taken up by the budget of the health insurance, but should be covered by other public organisations. Also for these costs estimates have been made, but without necessarily knowing all the parameters influencing them.

The individual recommendations and proposed measures for a Belgian Plan for Rare Diseases are listed in the table of content which precedes this summary and are described in more detail further on in this document.

Recommendations for a Plan

This document is a summary of an extended multi-stakeholder consultation set up by the Fund for Rare Diseases and Orphan Drugs. Several hundreds of people have contributed: many have been involved during the discussions in the working groups[3], others have participated to one of the seminaries and workshops which have been organised by the Fund in preparation of these proposals. Examples are the workshop 'Living with a Rare Disease – Consultation on Patient Empowerment', the 'Forum on Rare Disease Research in Belgium', or the colloquium 'Care and Cure for Rare Diseases: Societal and Ethical Aspects'.

The members of the Fund for Rare Diseases and Orphan Drugs are convinced that these recommendations and proposals can form the basis for the measures that the Minister of Social Affairs and Public Health will include in the final Belgian Plan for Rare Diseases.

The challenge: towards good practices as the norm

A rare disease is defined by the EU as a chronically debilitating and/or life-threatening disease with a prevalence fewer than 5 in 10,000 in the Community. There are no precise figures on the number of people affected by rare diseases in the EU, nor in Belgium, because of the failure of collecting data on them. Nevertheless, it has been recognised by EU governmental bodies – the Parliament, the Commission and the Council – and the Belgian Parliament that patients with a rare disease have specific needs because of the rarity of their disorder. In general, most patients with a rare disease are not making optimal use of the health and social care resources because of delays in diagnosis or even misdiagnosis, fragmented care, a lack of information and communication, limitations of effective treatment options, a shortage of guidelines on effective management of conditions, administrative hurdles, etc.

Nevertheless, it is certainly not all bad. On the contrary. numerous examples – both outside and within Belgium – demonstrate that high quality services and support to people with rare diseases are possible, and for a reasonable cost. For example the 8 Belgian Centres for Human Genetics play an important role in the diagnosis of patients with a rare disease and provide a state-of-the-art genetic consultation. Belgium also has 21 multidisciplinary Reference Centres for specific rare diseases or groups of rare diseases (6 Centres for Neuromuscular Disorders, 7 Centres for Cystic Fibrosis, and 8 Centres for Hereditary Metabolic Diseases).

3 A full list of the persons who participated to this process can be found in addenda 9 and 10.

Apart from these centres, expertise on many specific rare diseases is available in many Belgian university and peripheral hospitals or clinics.

Furthermore, Belgian patients currently have access to 43 reimbursed orphan drugs (some of them are life-saving), and many other drugs necessary for their treatment. Close to 150 patients' organisations are active in Belgium around rare diseases, one alliance organisation, RaDiOrg.be is grouping 80 different patients' organisations, and is the official representative of Eurordis in Belgium.

With a proper strategic approach, secured in a Belgian Plan for Rare Diseases, we can move towards a situation in which a high-quality, patient oriented and well-coordinated management of the needs of rare disease patients can become the norm, rather than the exception.
Necessarily, things have to change, but with these proposals, the members of Fund for Rare Diseases and Orphan Drugs call upon the goodwill of all concerned, to make these changes happen….

Five overarching principles

The current 42 proposals cover 5 main principles:

'Rarity' demands for specialisation and an integrated approach

Expertise and multidisciplinarity – the cornerstone of these proposals is the concentration of expertise in dedicated Centres employing a multidisciplinary and global approach to the management of rare disease patients. This includes medical, paramedical, rehabilitation, psychological and social care.

Building networks around 'rarity'

Collaboration and networking – in the case of rare diseases, joint working is essential due to the small numbers of patients affected by each rare disease, especially those at the very rare end of the spectrum. Therefore these recommendations appeal to the will of all concerned to collaborate and to network:
at the micro-level – which is the level of the individual patient around whom a functional network of care providers in and outside of the dedicated Centres should be built.
At the meso-level – which is the level of the future Belgian Plan for Rare Diseases.
At the macro-level – which is the level of collaboration across Europe and internationally.
It is essential that key stakeholder groups, including patients and patients' organisations, as vital sources of information and experience, are systematically engaged as partners in this process.

'Rare' should not be synonymous for 'unknown', and thus 'unloved'.

Knowledge, information and awareness – deepening the knowledge on rare diseases by intensifying epidemiological, basic, translational, clinical and social research, is essential. The setup of registries (general and disease specific) is in that respect a priority.
But, at least as important, is to spread the existing knowledge on rare diseases more widely. Information provision towards patients and their families should be improved and the awareness on rare diseases among peripheral care professionals and the public needs to be increased.

'Rare', but equal

Equity in access – patients with a rare disease deserve equal access to care, treatment and rehabilitation compared to other patients.

Also 'rarities' should properly be managed

Governance and sustainability – improving the health care of rare disease patients implies allocation of funds for the delivery of improved health and social services over the long term, as well as funding to implement the adaptation of the health system, including the establishment of new structures and/or new tasks, to respond to the unfulfilled needs of rare disease patients. In the current proposals, a timeframe of 5 years is foreseen (2012-2016). In the RIZIV/INAMI budget of 2011 a specific budget was already foreseen covering the costs of the implementation of a number of measures which were proposed during Phase I of the work done by the members of the Fund.

Monitoring the outcomes and effectiveness of a national comprehensive and integrated strategy for rare diseases will require the development of assessment and measuring instruments. Implementation and adjustment of the measures included in the final Belgian Plan for Rare Diseases will require a powerful advice and monitoring platform informing and assisting the Minister.

The measures in a nutshell

Expertise and multidisciplinarity

The provision of expertise centres at national level is considered the most effective instrument to offer high quality care to rare disease patients. They allow for the concentration of knowledge and expertise and the definition of diagnostic, healthcare and social care pathways. Centres should become hubs for collaboration and coordination of diagnosis and care, as well as for research, information provision and training of professionals. The formal acknowledgment and monitoring of these Centres would enable the decision makers to identify where to allocate specific resources.

The Fund for Rare Diseases and Orphan Drugs proposes three structures to combine national expertise while encouraging networking at European level: Centres of Expertise (CE), Centres for Human Genetics (CHG), and a Liaison network for Rare Diseases (LRD):

The first proposed network are the Centres of Expertise (CEs), bringing together all necessary expertise on a specific rare disease or a group of rare diseases. These Centres should be responsible for the global disease management of the patient in a multidisciplinary environment. This includes medical and paramedical treatment, but also the social aspects. In these Centres rare disease patients are expected to be assisted by care coordinators who constitute the link between the patient and all the medical, paramedical and social care professionals, both within and outside of the Centre of Expertise.

The second network structure should be formed by the Centres for Human Genetics (CHG), which have specific expertise in diagnosing rare diseases with a genetic background and in organising genetic counselling. It is anticipated by the members of the Fund for Rare Diseases and Orphan Drugs that the role of the CHGs in the field of rare diseases will be consolidated and even be strengthened on certain aspects.

Finally, there is the network of Liaison centres Rare Diseases (LRD). It should provide a supplementary safety net for patients who slip through the net of the CEs and CHGs. The LRD will de facto be located in the (university) hospitals which meet certain criteria. They should form a network of diagnostic and treatment units performing a multidisciplinary rare disease consultation coordinated by a medical liaison officer for rare diseases. LRDs are also responsible for the follow up and monitoring of patients who cannot be diagnosed or treated in a Belgian Centre of Expertise.

It is the ambition of these proposals that 5 years after the implementation of the first measures, approximately 15.000 patients would be treated in Belgian Centres of Expertise and 3.000 patients in such Centres abroad. These numbers are on top of the 3.000 to 4.000 patients who are currently treated in the Reference Centres and the 10.000 patients who are yearly seen in the Centres for Human Genetics. Furthermore, it is expected that the LRD network will yearly see approximately 2.000 patients for a multidisciplinary rare disease consultation.

The budget needed for the set up and running of the Centres of Expertise forms the bulk of the expenses of all the 42 measures. The previewed budget in the fifth year after the first implementation, when all foreseen CEs should be operational, would be approximately 36 million Euro per year (including the financing of the function of the care coordinator). This is close to 80% of the total yearly budget for all proposed measures together. In comparison, the foreseen budget for the LRD network in the same year would be limited to 1 million Euro per year (<2,5% of the total yearly budget).

The creation of CEs and LRD, together with a consolidation of the role of the CHGs, has various impacts on the patients. The main impact is at the level of diagnosis, treatment and patient support, resulting in an improved quality of life for patients and their relatives. The coordination of the patient's medical and non-medical care and social support is taking place in a multidisciplinary environment with medical, paramedical, psychological and social care expertise.
At the same time, general practitioners and local specialists would be able to easily identify the appropriate health care resources for their case. They would have structural access to expert opinions, and would get involved in the application of treatment plans and clinical and social pathways.

Proposals for measures which fall under 'Expertise and multidisciplinarity' include measures:

1.1. Creation of Centres of Expertise
1.2. Strengthen the role of the Centres of Human Genetics
1.3. Creation of the network of Liaison centres Rare Disease
8.1. The creation of the function of the rare disease care coordinator
8.2. Facilitate the access to specialised help and simplify administrative procedures

Collaboration and networking

Networking is an asset for quality care of rare diseases. Patients with a rare disease will get better treatment if good practice diagnostic and therapeutic approaches are shared between Centres at national and international level, but also between Centres and peripheral care services. A number of measures have been proposed to enhance collaboration and networking between the various parties involved.

Also the relation between patients and professional caregivers deserves attention, as well as the networking possibilities between patients and their representing organisations with professional caregivers and decision makers. Patients and patients' organisations are without doubt a vital source of information and experience. Furthermore patients' organisations are a crucial actor in the empowerment of patients with a rare disease. They play an important role in offering information and assistance to patients. And patients with rare diseases have in many cases played an active and instrumental role in determining research projects and shaping health care policy. Therefore, it is advisable to put processes in place to engage systematically with these groups in a partnership to achieve the goals set forward in the future Belgian Plan for Rare Diseases. At the same time, patients' organisations are called to intensify their mutual collaboration.

Proposals for measures which fall under 'Collaboration and networking' include measures:

1.4. Networking between Centres at national level
1.5. Networking between Centres and peripheral care services
1.6. Networking at European and international level
4.1. Empower patients
4.2. Enforceable patient participation
4.3. Improvement of collaboration between patient organisations
4.4. Development of a medical passport
10.1. Creation of a Platform for Rare Diseases

Knowledge, information and awareness

How can knowledge on rare diseases be increased? There are several answers: current knowledge should be deepened by research; existing knowledge should be communicated broader through the exploitation of various (new) information channels; proper training possibilities should be foreseen for both professional caregivers and staff members of patients' organisations; and lastly the public at large should be made aware of the existence and specificities of rare diseases. Therefore, not less than 14 proposals are dealing with this topic.

To learn more about rare diseases, the existence of an accurate inventory of rare diseases, regularly updated, by prevalence, mechanism, clinical features and aetiology would provide a necessary documentary support to health care providers, patients and researchers. Secondly, basic, translational and clinical research on rare diseases is scattered throughout the EU and is comparatively scarce with respect to the high number and heterogeneity of rare diseases. The main problems are the limited number of patients for each disease and/or the lack of specific resources. But, as has been shown in the past, the outcomes of research on rare diseases can also have significant impacts on other, more common diseases. So there is a strong need for fostering collaborative programs at national, European and international level on all fields of research on rare diseases, from fundamental/basic, over epidemiological, translational and clinical to social research.

Patients with rare diseases, their families, and their local treating caregivers, experience major difficulties in finding information on their disease (especially in their own language). It is necessary to plan a reliable tool for the communication of practical information to patients and health professionals. A portal website dedicated to rare diseases should become an important communication instrument. This website should link to validated information sources on the organisation of care and specialised services, on orphan drugs and other treatments, on-going experimental trials, rehabilitation and social services, administrative and legal information on access to care, right to reimbursement and other benefits provided by the public services. This website should also have links to Orphanet, websites of patient organisations and information on for patients with chronic diseases.

Furthermore, the adoption of appropriate initiatives for training and education of health professionals is an important mechanism to improve diagnosis and quality of care. The need for training does not only refer to clinical capacity, but also to the ability to communicate with patients and the proper management of the patient's needs.

Finally, addressing the communication challenge is essential for the success of any national plan or strategy for rare diseases. Because of their rarity, rare diseases are unknown. So there is the major issue of the awareness on rare diseases, at the level of the general public as well as among the professional caregivers. Furthermore,

most proposed measures need to be known by those who are involved in their implementation as well as those who might benefit from them. Setting up new structures, without making them widely known, would mean poor utilisation of resources. Therefore, one of the main tasks after the implementation of the future Belgian Plan for Rare Diseases is the elaboration of a long term (5 years) communication strategy.

In the current proposals, the aggregate budget for 'knowledge, information and awareness', including stimulation programs for research, is estimated to be approximately 16 million Euro over a period of 5 years. In some years budgetary emphasis is on impulse programs for research, in other years on awareness campaigns.

Proposals for measures which fall under 'Knowledge, information and awareness' include measures

2.1. Central Registry for Rare Diseases
2.2. Disease specific registries
3.1. Portal information website
3.2. Support for Orphanet Belgium
3.3. Development of a communication plan
5.1. Education and teaching on rare diseases and orphan drugs
5.2. Continued training on rare diseases
7.1. Information service of clinical trials, compassionate use and medical need programmes
7.5. Stimulation of academic clinical trials for rare diseases
9.1. Identification and traceability of rare disease research
9.2. National support to E-rare
9.3. Impulse programme for research on rare diseases
9.4. Identification of unmet medical needs
9.5. Public funds for translational research

Equity in access

It was already mentioned how rare disease patients have sometimes spent years wandering through the maze of the health system to find an accurate diagnosis and how some are fighting to obtain life-saving treatments or to be reimbursed by their health authorities. The members of the Fund for Rare Diseases and Orphan Drugs have defined a number of obstacles in the organisation of the Belgian – and EU – health care system which hamper the access to equal care, as experienced by rare disease patients.

Proposals are made for improving access to diagnostic tests (performed within and outside of Belgium), to clinical trials, and to compassionate use and medical need programmes. Also proposals for setting up a system of early access to orphan drugs, including early temporary reimbursement, have been defined. As well as proposals on the use of materials for compounding used to treat rare diseases, on responsible off-label use of drugs and on home treatment under clear conditions. Also on the role of the Special Solidarity Fund, the role of the Colleges for Orphan Drugs and on the improvement of the procedures used by ethics committees, recommendations have been made.

Lastly, Belgian representatives at appropriate European bodies (including EUCERD, EMA,…) are expected to take an active, and even leading role, in several EU dossiers, including the revision of the EU Clinical Trial Directive; a revision of the criteria used to grant orphan designation when appropriate materials for compounding are available and used; issues on early access, early reimbursement and efficient monitoring following market authorisation; and on transparency on the use of medical devices for patients with a rare disease.

Especially the first measures – access to tests and early access/early reimbursement of orphan drugs – can have a significant budgetary impact. I.e. the proposal on improved access to appropriate diagnostic tests is estimated to cost 1,3 million Euro per year in the fifth year of implementation of the future Belgian Plan. Setting up a system of early access and early reimbursement would represent a recurrent yearly cost of 3,5 million euro.

Proposals for measures which fall under 'Equity in access' include measures:

6.1. DNA samples tested abroad
6.2. Non-DNA testing
7.1. Information service of clinical trials, compassionate use and medical need programmes
7.2. Adaptation of legislation on information on compassionate use and medical need programmes
7.3. Application of the voluntary harmonised procedure
7.4. Single opinion of ethics committees
7.6. Role of the Special Solidarity Fund
7.7. Conditions for the use of pharmacy prepared drugs (materials for compounding)
7.8. Early access to and early reimbursement of orphan drugs
7.9. Role of the Colleges for Orphan Drugs
7.10. Responsible off-label use of drugs
7.11. Home treatment under clear conditions
7.12. Patient adherence to treatment
7.13. European issues related to access to treatment

Governance and sustainability

For each of the proposed measures, the budgetary impact was estimated over a period of six years (2011-2016). These estimates were calculated in consultation with specialists from RIZIV/INAMI. A more detailed budget impact analysis is included in chapter 5 and annex 8 of the Recommendations and proposed measures for a Belgian Plan for Rare Diseases.

An important issue is the monitoring of the outcomes and effectiveness of the proposed measures. This will not only require the development of assessment and measuring instruments, but also the establishment of a strong managerial structure, which can inform and assist the Minister and the administrative bodies involved in the implementation and the follow up.

The members of the Fund for Rare Diseases and Orphan Drugs therefore advise the setup of a Platform for Rare Diseases, which could be helpful in the process of implementation, coordination and monitoring of the future Belgian Plan for Rare Diseases. One of the tasks of this Platform would also be to further assess the societal and ethical issues involved in rare diseases in order to guarantee the sustainability of the measures.

Proposals for measures which fall under 'Governance and sustainability' include measures

10.1. Creation of a Platform for Rare Diseases
11.1. Ethical issues: transparency of pricing of orphan drugs and other treatments
11.2. Citizens consultations on rare diseases and orphan drugs

The Fund for Rare Diseases and Orphan Drugs

The Fund for Rare Diseases and Orphan Drugs, was created by a group of stakeholders under the presidency of Prof. em. Jean-Jacques Cassiman and is managed and financially supported by the King Baudouin Foundation.

The Fund has always aimed to take a collaborative approach and has brought around the table all relevant actors in the field of rare diseases and orphan drugs in order to draw up these proposals for measures for a future Belgian Plan for Rare Diseases. The focus was the improvement of the lives of patients with a rare disease and of their relatives.

1. STRATEGIC OBJECTIVES AND TARGET GROUP

Vision and objectives

1.1. Because of their low prevalence, their seriousness and their specificity, rare diseases call for a global approach based on special and combined efforts to prevent significant morbidity or avoidable premature mortality, and to improve the quality of life and socioeconomic potential of affected persons. Of paramount importance for patients with rare diseases are the principles and overarching values of universality, access to good quality care, equity and solidarity which are used throughout the EU Health Systems.[4]

Characteristics of rare diseases [5]

Rare diseases are characterised by a broad diversity of disorders and symptoms that vary not only from disease to disease but also from patient to patient suffering from the same disease. Relatively common symptoms can hide underlying rare diseases, leading to misdiagnosis:

- *rare diseases are often chronic, progressive, degenerative, and life-threatening;*
- *rare diseases are disabling: the quality of life of patients is often compromised by the lack or loss of autonomy;*
- *high level of pain and suffering for the patient and his/ her family;*
- *often there is no existing effective cure;*
- *there are between 6000 and 8000 rare diseases;*
- *75% of rare diseases affect children;*
- *30% of rare disease patients die before the age of 5;*
- *80% of rare diseases have identified genetic origins. Other rare diseases are the result of infections (bacterial or viral), allergies and environmental causes, or are degenerative and proliferative.*

1.2. In line with the Communication on rare diseases from the European Commission[6], the European Council Recommendation[7], and a request by Ms. Laurette Onkelinx, Belgian Minister of Social Affairs and Public Health [see chapter 2], the Fund for Rare Diseases and Orphan Drugs, hosted by the King Baudouin Foundation[8], has worked out a number of recommendations and proposals which could form the basis for a Belgian Plan for Rare Diseases.

4 *Council Conclusions on Common values and principles in European Union Health Systems, Official Journal of the European Union, 2006/C 146/01, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2006:146:0001:0003:EN:PDF*

5 *Characteristics of rare diseases, website Eurordis, http://www.eurordis.org/content/what-rare-disease*

6 *Communication from the Commission on Rare Diseases: Europe's Challenges, sec(2008)2713, http://ec.europa.eu/health/ph_threats/non_com/docs/rare_com_en.pdf*

7 *Council Recommendation on an action in the field of rare diseases, Official Journal of the European Union, 2009/C 151/02, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF*

8 *Fund Rare Diseases and Orphan Drugs, http://www.kbs-frb.be/fund.aspx?id=223930&LangType=1033*

The aim of this Plan should be to improve the access and equity to prevention, diagnosis, treatment and rehabilitation for patients suffering from rare diseases; to increase the effective and efficient recognition of rare diseases; to promote the research for rare diseases and the development of new treatments and effective orphan medication; and to involve patients and their associations in the constructive thought processes and decision-making about rare diseases and orphan drugs.

Proposals in two phases [9]

The recommendations and proposals for the Belgian Plan for Rare Diseases were drafted in two Phases. Phase I – which was presented to the Minister in May 2010 – focused on a number of measures which could be implemented early.[10] *Some of these proposals have in the meantime been supported by the Minister of Social Affairs and Public Health. Implementation of these proposals was – during the drafting of the current document – in progress.*

This document proposes an integrated set of recommendations and measures in order to support the Minister in drawing up a comprehensive Belgian Plan for Rare Diseases. The measures proposed during Phase I of the work of the Fund are therefore part of this document, and were fine-tuned and updated if necessary. During Phase II, 8 workgroups have outlined supplementary proposals to obtain an integrated national strategy for patients with a rare disease.

1.3. These recommendations and proposals for a Belgian Plan for Rare Diseases have the intention to defragment the current offer of services, enable patients and health professionals to have access to and to provide best practice care, stimulate the research into novel diagnostic techniques and treatments, facilitate the access to proper medication, raise the public and political awareness about rare diseases….

1.4. Main objectives of the proposals for a Belgian Plan for Rare Diseases are to:

- reduce the delay of diagnosis and decrease the number of misdiagnoses;
- increase the quality of care (medical and non-medical) patients receive;
- stimulate the development of and access to new treatments (better than existing, or new for those diseases where no treatments exist);
- increase the knowledge base on rare diseases;
- improve the quality of life of patients and families;
- create higher awareness among all stakeholders, which should lead to earlier diagnosis and increase access to expertise;
- stimulate fundamental research and clinical studies.

9 *Characteristics of rare diseases, website Eurordis, http://www.eurordis.org/content/what-rare-disease*

10 *Recommendations and proposed measures for the Belgian Plan for Rare Diseases – Phase I, 2010, Fund Rare Diseases and Orphan Drugs, managed by the King Baudouin Foundation, http://www.kbs-frb.be/uploadedFiles/KBS-FRB/05)_Pictures,_documents_and_external_sites/09)_Publications/PUB_2025_BelgianPlanForRareDiseases_EN_02_DEF.pdf*

1.5. Additional objectives:
- identify and concentrate expertise;
- identify patients and create links between patients and experts;
- ensure treatments are performed according to best practice principles (if possible based on clinical evidence);
- ensure patient management is performed in multi-disciplinary environments (as a condition for high quality of care);
- stimulate the inclusion of Belgian expert centres in research programs (including clinical trials) in order to increase (clinical) evidence and develop innovative diagnostics and treatments;
- improve the processes to get adequate social and financial support from public instances.

1.6. Supporting objectives:
- organise networks between all stakeholders at national level;
- organise links between Belgium and other countries on the management of patients with a rare disease (avoid duplication, ensure contribution by Belgium to EU and other international initiatives and tools);
- evaluate all measures and proposals from an ethics perspective.

1.7. According to the European recommendations, a National Plan for Rare Diseases consists of a set of integrated and comprehensive health policy actions to be developed and implemented at national level.[11] It should have well specified objectives and actions to be supported by a budget, implemented within a time frame, and evaluated with specific indicators.
'Integrated' refers to the fact that strategies should be developed in a way to identify complementarities, maximize synergies and avoid duplications.
'Comprehensive' refers to the fact that the actions foreseen in the plan should fulfil all main patients' needs (e.g. quality of care but also social services).

1.8. The intention of these recommendations and proposed measures for a Belgian Plan for Rare Diseases is to eliminate inequalities in health care, paramedical and social care, and personal development opportunities arising from the rareness of these severe diseases.

Definitions

1.9. Definition of a rare disease – **Rare diseases are life-threatening or chronically debilitating diseases which are of such low prevalence that special combined efforts are needed to address them. As a guide, low prevalence is taken as prevalence of less than 5 per 10.000 in the Community**.
This definition was first stipulated in Regulation 141/2000[12] of the European Parliament and the Council on orphan medicinal products and was later on confirmed by the Health and Consumer Protection Directorate-General of the European Commission[13].

11 *Recommendations for the development of National Plans for Rare Diseases, Guidance document, EUROPLAN, p. 12, http://www.europlanproject.eu/public/contenuti/files/Guidance_Doc_EUROPLAN_20100601_final.pdf*

12 *Regulation (EC) no 141/2000 of the European Parliament and of the Council of 16 December 1999 'On orphan medicinal products', http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:018:0001:0005:en:PDF*

13 *Useful information on rare diseases from an EU perspective, European Commission Health & consumer protection directorate-general, http://ec.europa.eu/health/ph_information/documents/ev20040705_rd05_en.pdf*

1.10. Definition of an orphan drug – An orphan drug is a medicinal product that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10.000 persons in the Community when the application is made, or that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the Community and that without incentives it is unlikely that the marketing of the medicinal product in the Community would generate sufficient return to justify the necessary investment; and that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorised in the Community or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition.[14]

1.11. The field of rare diseases is vast and complex. This has been reported in several important European documents[15] and is confirmed by Orphanet, the European portal for rare diseases and orphan drugs[16], and Eurordis, the largest non-governmental patient-driven European alliance of patients' organisations and individuals active in the field of rare diseases[17].
In particular it is underlined that:

- rare diseases include hereditary diseases (likely 80% of rare diseases have a genetic background), rare cancers, auto-immune diseases, congenital malformations, toxic and infectious diseases and others;
- while 5 in 10.000 seems very few, in a total population of 10.000.000 Belgian citizens, this could mean as many as 5.000 patients for a single disease. However it should be underlined that the number of rare disease patients varies considerably from disease to disease, and that most rare diseases only affect a few dozen patients or sometimes even less;
- although every single disease is rare, between 6.000 and 8.000 rare diseases have been described.[18]

1.12. Not all diseases in the Orphanet prevalence list are however life threatening or debilitating for all patients who are affected by them:

- some diseases have a rather mild course in some patients;
- other groups of patients with a rare disease are already diagnosed and treated within the existing health care system according to high standards. The (medical and other) need of these patients for supplementary expert diagnosis or specialised and dedicated treatment regimes, is rather low;
- some patients may already benefit from dedicated measures and health care structures set up in the context of other policy actions (i.e. the Belgian Cancer Plan, the Programme for Chronic Diseases,…).

14 *Regulation (EC) no 141/2000 of the European Parliament and of the Council of 16 December 1999 'On orphan medicinal products', http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:018:0001:0005:en:PDF*

15 *Communication from the Commission on Rare Diseases: Europe's Challenges, sec(2008)2713, http://ec.europa.eu/health/ph_threats/non_com/docs/rare_com_en.pdf and Council Recommendation on an action in the field of rare diseases, Official Journal of the European Union, 2009/C 151/02, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF*

16 *Orphanet, http://www.orpha.net*

17 *Eurordis, Rare Diseases Europe, http://www.eurordis.org/*

18 *Prevalence of rare diseases: bibliographic data, Orphanet Report Series, Rare Diseases collection, November 2010, http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_decreasing_prevalence_or_cases.pdf*

Target population

1.13. The target population of the Belgian Plan should be **all individuals, of either sex, at any moment in their life, affected by a rare disease (see §1.9.), and who experience a specific need which is not sufficiently covered by the current medical, paramedical and/or social care system**.

1.14. As long as there is no formal registry for rare diseases, it is difficult to estimate the total number of patients and families who could benefit from the future Belgian Plan for Rare Diseases. While the prevalence of congenital anomalies is about 3% of the new-borns, those surviving and suffering from chronic, severe and/or life threatening rare diseases can be roughly estimated at between 60.000 and 100.000 patients in the total population of Belgium. This is likely to be the size of the total target population.

1.15. The ambition of these recommendations and proposed measures is to treat approximately 18.000 patients with rare diseases during the first 5 years of its implementation – on top of the 3.500 to 4.000 patients who are currently being treated in the existing reference centres (centres with a RIZIV/INAMI-convention) and the 10.000 patients who are yearly seen in one of the eight Centres for Medical Genetics.
It is estimated that 15.000 patients will be treated in Belgian Centres of Expertise, 3.000 patients in Centres abroad.

Methodology

1.16. The Fund for Rare Diseases and Orphan Drugs was founded by a group of stakeholders under the presidency of Professor Jean-Jacques Cassiman. The Fund is managed and financially supported by the King Baudouin Foundation. The Fund was asked by Ms. Laurette Onkelinx, Minister of Social Affairs and Public Health, to develop a number of recommendations and proposals which could form the basis of a future Belgian Plan for Rare Diseases.
The Fund has always pursued a collaborative approach. During the preparation of these 'Recommendations and proposed measures for a Belgian Plan for Rare Diseases' all relevant actors in the field of rare diseases and orphan drugs have been closely involved.
Central in this process were the multistakeholder groups responsible for a specific work package. These packages were divided as follows:

1. National registry, disease specific databases and European collaboration
2. Identification of non-medical costs for the patient/Comprehensive care
3. Information/Patient empowerment
4. Centres of Expertise/Collaboration and networking at national level (including neonatal screening)
5. Access to diagnosis, drugs and medical treatment
6. Stimulation of (fundamental) research

6.B. National and international networking and collaboration with regard to therapy and patient management

6.C. Improvement of clinical research, including clinical trials

7. Education and formation of professional caregivers

These working groups included representatives from (not limited list) physicians and geneticists, patients' organisations, RIZIV/INAMI, Federal Public Service (FOD/FPS) Health, Food Chain and Environment, Federal Agency for Medicines and Health Products (FAGG/AFMPS), Belgian Scientific Institute for Public Health (WIV/ISP), Sickness Funds, Hospital Pharmacists, medical management of University Hospitals, Pharma.be, services of neonatal screening,…. The complete composition of the working groups is included in annex 10.

All recommendations and proposals were formulated, discussed and selected between June 2009 and April 2011. A first series of proposals was already presented to the Minister in May 2010. The document presented here, however, represents the result of the complete working process over 24 months (June 2009 - May 2011).

Each working group had the freedom to research, to capture themes and to formulate proposals according to its own insights and methods. Results were discussed and evaluated regularly by the Management Committee of the Fund for Rare Diseases and Orphan Drugs. The composition of this committee is included in annex 9. During the 24 month process, five sessions were organised which were open to all members of the different working groups. During these sessions all (preliminary and definitive) results were presented and discussed in plenum.

The last version of these 'Recommendations and proposed measures for a Belgian Plan for Rare Diseases' were approved by the members of the Management Committee on 10 May 2011.

2. THE CONTEXT… LOOKING AFTER THE MOST VULNERABLE

International context

2.1. A national approach with integrated and comprehensive strategies for rare diseases on the one hand and an increased collaboration with the development of common solutions at EU level[19] on the other hand, are key to improve health and social care of patients with rare diseases. In this context, the **Commission Communication on rare diseases** and the **Recommendation from the European Council** states that Member States **should establish and implement plans and strategies for rare diseases by 2013 in order to improve the access and equity to prevention, diagnosis, treatment and rehabilitation for patients suffering from rare diseases**.[20]
A Eurobarometer survey published on 28 February 2011 reveals widespread support for action on rare diseases at EU level. 95% of respondents believe there should be more European cooperation in this area and that rare disease patients should have the right to access appropriate care in another Member State. Approximately 2 out of every 3 respondents know that rare disease affect a limited number of people and require very specific care.[21]

National context

2.2. On February 19, 2009 the Belgian House of Representatives adopted a resolution submitted by Yolande Avontroodt, Katia Della Faille, and Herman De Croo concerning an action Plan on Rare Diseases and Orphan Drugs.[22]

2.3. The Fund Rare Diseases and Orphan Drugs, hosted by the King Baudouin Foundation[23] was asked by Ms. Laurette Onkelinx, Minister of Social Affairs and Public Health to play a coordinating role in the editing of recommendations and proposals for a Belgian Plan for Rare Diseases. The Fund brings together the various stakeholders involved in all aspects of rare diseases as well as the development and availability of orphan drugs.

19 *Cross-border care, European Commission, Public Health, http://ec.europa.eu/health/cross_border_care/policy/index_en.htm and Directive of the European Parliament and of the Council on the application of patients' rights in Cross-border healthcare, http://register.consilium.europa.eu/pdf/en/11/pe00/pe00006.en11.pdf*

20 *Communication from the Commission on Rare Diseases: Europe's Challenges, sec(2008)2713, http://ec.europa.eu/health/ph_threats/non_com/docs/rare_com_en.pdf and Council Recommendation on an action in the field of rare diseases, Official Journal of the European Union, 2009/C 151/02, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF*

21 *European awareness of Rare Diseases, Special Eurobarometer 361, http://ec.europa.eu/health/rare_diseases/docs/ebs_361_en.pdf*

22 *Resolutie betreffende een actieplan inzake zeldzame aandoeningen en Weesgeneesmiddelen - Résolution relative à la mise en oeuvre d'un plan d'action en ce qui concerne les affections rares et les médicaments orphelins, Belgian House of Representatives, DOC 52 0505/005, http://www.dekamer.be/FLWB/pdf/52/0505/52K0505005.pdf*

23 *Fund Rare Diseases and Orphan Drugs, http://www.kbs-frb.be/fund.aspx?id=223930&LangType=1033*

2.4. In 2008, Ms. Laurette Onkelinx, Minister of Social Affairs and Public Health announced a Programme for the amelioration of the life quality of patients with a chronic disease.[24] Patients with a rare disease may benefit from the initiatives which will be developed in the framework of this action plan. The recommendations and measures proposed in this document will therefore be further developed and implemented in consultation with the agencies responsible for the supervision and implementation of the measures described in the Programme for Chronic Diseases. Patients with a rare cancer can in most cases make use of the measures included in the Cancer Plan.[25] A good coordination and collaboration between the future Belgian Plan for Rare Diseases, The Cancer Plan and the Programme for chronic diseases is therefore indispensable.

Current situation in Belgium on…

… medical expertise

2.5. Belgium already has a number of 'dedicated centres' which are dealing with rare disease patients. These are 8 Centres for Human Genetics and 21 multidisciplinary Reference Centres: 6 centres for neuromuscular disorders, 7 centres for cystic fibrosis, and 8 centres for hereditary metabolic diseases. The Reference Centres have a 'convention' (a contract) with RIZIV/INAMI which is renegotiated regularly.

2.6. The Centres for Human Genetics have been created and are functioning under the legal base of the Royal Decree of 14 December 1987 establishing the Centres for the purpose of diagnosis of constitutional genetic disorders. Each of the seven Belgian university hospitals has a Centre for Human Genetics. The eighth Centre, the 'Institut de Pathologie et de Génétique' in Gosselies, is an independent institute and has no direct link to a hospital or university.
Since 80% of the rare diseases have a genetic basis, and since 90% of the genetic conditions are rare, the Centres for Human Genetics are, with a total yearly number of patients contacts of approximately 10.000, an important actor in the clinical management of patients with a rare disease, especially at the levels of diagnosis and genetic counselling.
The Belgian Centres for Human Genetics have a full service offering, i.e. they offer different types of tests and technologies, and patient and family counselling. Their expertise and their unique position in the diagnosis and management of patients with a rare disease is fully acknowledged in these proposals for a Belgian Plan for Rare Diseases. Furthermore, their role as expert centres for the diagnosis of many rare diseases is unquestionable.

2.7. Apart from the Reference Centres and the Centres for Human Genetics, expertise on rare diseases is available in many Belgian university and peripheral hospitals or clinics. Unfortunately, this expertise is not well known to the public and to the general practitioners. The services within these hospitals may not interact between them or with similar expert centres in Belgium or abroad, many of the services are fragmented, lack structure and official recognition.
Furthermore, regionalization of neonatal screening has resulted in different approaches in the regions and different procedures of follow up on the identified families, which may need a more harmonized approach.

24 *Prioriteit aan de chronisch zieken!, Programma voor de verbetering van de levenskwaliteit van personen met chronische ziekten, 2009-2010, http://www.laurette-onkelinx.be/articles_docs/20080923_-_propositions_malades_chroniques_N.pdf and Priorité aux malades chroniques!, Programme pour l'amélioration de la qualité de vie des personnes atteintes d'affections chroniques, 2009-2010, http://www.laurette-onkelinx.be/articles_docs/20080923_-_propositions_malades_chroniques_F.pdf*

25 *Plan National Cancer - Nationaal Kankerplan, http://www.laurette-onkelinx.be/articles_docs/32_initiatieven_N.pdf*

… access to appropriate medication

2.8. Pharmaceutical treatments for rare diseases were – at least in the past – less likely to be produced by companies because the market is small and the development costs are not necessarily lower compared to medicines developed for more common diseases. Both in the US and in the European Union incentives have been created to promote research and development on orphan drugs. To qualify for the special regulatory arrangements for orphan drugs in the EU, a project for a drug has to obtain the orphan status through the orphan designation procedure at EMA, the European Medicines Agency. Afterwards, when the drug is ready for market introduction, EU marketing authorisation must be applied for through the centralized procedure at the EMA. Between 2000 and February 2011 more than 820 medicinal products under development received European orphan drug status[26], 63 received marketing authorisation[27]. With 63 orphan drugs available in the EU, it is clear that at the moment, only a small part of the need for specific medical treatments of rare diseases is covered.

2.9. Each EU member state negotiates pricing and reimbursement separately with the pharmaceutical companies providing orphan drugs. Despite the incentives for orphan drugs development and registration, access to orphan drugs in the EU member states may be very variable. Regulation and orphan drug reimbursement decisions at Belgian level are taken by the Minister of Public Health and Social Affairs, after advice from the Drug Reimbursement Committee, the Finance inspector and upon approval by the Minister of Budget. Orphan drugs follow the same procedure as Class I pharmaceutical products, i.e. products for which the company claims a therapeutic added value. However, unlike for Class I pharmaceutical products, no pharmacoeconomic evaluation has to be submitted for orphan drugs.

2.10. The expenditures of the Belgian National Institute for Health and Disability Insurance (RIZIV-INAMI) on orphan drugs are estimated to be approximately 66 million Euro in 2008[28] and 70 million Euro in 2009[29]. This was over 5% of the total hospital drug budget and further estimates indicate the future cost will be well above 10% of hospital drug budget in a number of few years from now.[30] Orphan drugs represent 2,6% of total drug reimbursement expenditures by RIZIV-INAMI in 2009. As of February 2011 the Belgian RIZIV-INAMI reimburses 42 orphan drugs. This number includes drugs for rare cancers.[31]

2.11. In Belgium prescription of orphan medication is the exclusive responsibility of an expert physician, i.e. a specialist physician in a specific discipline. The prescription and individual reimbursement of orphan drugs is subject to conditions. The treating specialist physician must first obtain the approval of a Medical Advisor of the patient's sickness fund to prescribe the medicine. The Medical Advisor can, but is not obliged to, request the

26 *Register of designated Orphan Medicinal Products, http://ec.europa.eu/health/documents/community-register/html/orphreg.htm, consulted on February 9, 2011.*

27 *Lists of Orphan Drugs in Europe, Orphanet Report Series, Orphan Drugs collection, January 2011, http://www.orpha.net/orphacom/cahiers/docs/GB/list_of_orphan_drugs_in_europe.pdf*

28 *Policies for Orphan Diseases and Orphan Drugs, Belgian Health Care Knowledge Centre, 2009. http://www.kce.fgov.be/index_en.aspx?SGREF=13035&CREF=13647*

29 *Personal communication by Céline Hermans, RIZIV/INAMI.*

30 *Denis A, Simoens S, Fostier C, Mergaert L, Cleemput I. Beleid voor zeldzame ziekten en weesgeneesmiddelen. Health Technology Assessment (HTA). Brussel: Federaal Kenniscentrum voor de Gezondheidszorg (KCE); 2009. KCE reports 112A (D/2009/10.273/30)/Denis A, Simoens S, Fostier C, Mergaert L, Cleemput I. Politiques relatives aux maladies rares et aux médicaments orphelins. Health Technology Assessment (HTA). Bruxelles: Centre federal d'expertise des soins de santé (KCE). 2009. KCE Reports 112B. D/2009/10.273/31.*

31 *List of reimbursed orphan drugs, RIZIV-INAMI, http://www.inami.fgov.be/drug/fr/drugs/orphan_drugs/index.htm , http://www.inami.fgov.be/drug/nl/drugs/orphan_drugs/index.htm*

advice of the 'College of Medical Doctors for Orphan Drugs' (CMDOD) if such a College exists for the disease or disease class for which the orphan drug would be used. In practice, all sickness funds have agreed to refer all requests to the CMDOD. Separate sub-Colleges exist for separate products. It is the Drug Reimbursement Committee that proposes to the Minister of Health whether or not such a sub-College should be established. Individual reimbursement advices to the medical advisors are taken on a case by case basis by the CMDOD[32]. In February 2011, there were subcolleges for 21 orphan drugs.[33]

2.12. If a medicinal product is not yet on the Belgian list of reimbursed pharmaceutical products or if the patient needs the medication for an off label indication, the patient may be able to benefit from a compassionate use or a medical need programme by the company. In case the drug is already on the market, the patient can request reimbursement through the Special Solidarity Fund (SSF) on condition that there is no College. Conditions for compassionate use, medical need or reimbursement through the SSF are defined by law.
The functioning and the efficiency of the Special Solidarity Fund were recently assessed by the Belgian Health Care Knowledge Centre.[34]

2.13. The distribution of orphan drugs in Belgium occurs mostly through hospital pharmacies.[35] In some other countries orphan drugs can also be delivered through community pharmacies.

… patients' organisations and contact with companions

2.14. Close to 150 patients' organisations are currently active in Belgium on the topic of rare diseases.[36] A number of these associations have websites. Some are member of regional platform organisations like the Vlaams Patiëntenplatform (VPP)[37] and the Ligue des Usagers des Services de Santé (LUSS).[38] In January 2008 the Rare Diseases Organisation Belgium (RaDiOrg.be)[39] was founded. RaDiOrg.be is a coordinating alliance of approximately 80 specific patients' organisations and is the official representative of Eurordis[40] in Belgium. Its mission is to increase the awareness in the general public of the existence of patients with a rare disease, to increase the quality of care, to inform the patient and his/her relatives, to provide social support for the patients and to stimulate research into the aetiology and treatment of these diseases. RaDiOrg.be created a web site to encourage the dissemination of information on rare diseases in Belgium. Under the High Protection of Her Royal Highness Princess Astrid, RaDiOrg.be organises the yearly Rare Disease Day (end of February).

32 *De vergoedbare weesgeneesmiddelen en de colleges, RIZIV, http://www.riziv.fgov.be/drug/nl/drugs/orphan_drugs/colleges.htm#3 or Les Médicaments orphelins remboursables et les Collèges, INAMI, http://www.riziv.fgov.be/drug/fr/drugs/orphan_drugs/colleges.htm#3*

33 *List of reimbursed orphan drugs with college, RIZIV-INAMI, http://www.inami.fgov.be/drug/fr/drugs/orphan_drugs/index.htm , http://www.inami.fgov.be/drug/nl/drugs/orphan_drugs/index.htm*

34 *Optimisation of the operational processes of the Special Solidarity Fund, KCE reports vol.133C, http://www.kce.fgov.be/index_en.aspx?SGREF=9470&CREF=16772*

35 *Only Glivec, Kuvan, Thalidomide, Tobi can be distributed without the intervention of the hospital pharmacist.*

36 *Information from RaDiOrg.be, http://www.radiorg.be/onze-leden/organisaties and Orphanet, http://www.orpha.net/consor/cgi-bin/SupportGroup_Search_List.php?lng=EN&type_list=SupportGroups_by_country&lng=EN&search=SupportGroup_Search_List&data_id=0&TAG=BE*

37 *www.vlaamspatientenplatform.be*

38 *www.luss.be*

39 *www.RaDiOrg.be*

40 *www.eurordis.org*

Specific needs of patients with a rare disease

2.15. According to Eurordis, European citizens affected by a rare disease can currently not necessarily rely on a coherent strategy for care and support in most member states. Due to the rarity of their conditions, health professionals often have limited or no experience in diagnosing, supporting and treating them. If appropriate services are existing, lack of communication, coordination and acquaintance often makes these services hard to access for patients and their relatives. Moreover, some conditions occur so infrequently that the cost of developing and bringing to the market a medicinal product to diagnose, prevent or treat the condition would not be recovered by the expected sales of the medicinal product. Under normal market conditions the pharmaceutical industry would be unwilling to develop medicinal products for rare diseases.

2.16. Several organisations [41] [42] [43] [44] have investigated the needs of Belgian patients with a rare disease (and their families) and the difficulties they experience. Summarised, these needs fall in the following categories:

- **more knowledge and recognition** – rare diseases are not always recognised by physicians; scientific knowledge is often limited or non-existing; societal recognition is low,…
- **decrease in delay of diagnosis and better information** – delayed and incorrect diagnosis; lack of specialised diagnostic centres or no timely referral to such centres; unequal and limited neonatal screening in Belgium;…
- **better access to high quality treatment and organisation of care system** – lack of centres of expertise; low cooperation between various health care providers; deficient availability of new medicines, paramedical and psycho-social care;…
- **lower costs of diagnosis and treatment** – price of orphan drugs and specialised medical devices; high costs for other medication (incl. D-medication) and cosmetics; social costs (disability and labour); hidden costs…
- **lack of epidemiological data and registration of patients**…
- **social integration of the patient with a rare disease** – difficulties with administrative statute; reduction of educational, professional and social opportunities; isolation and social exclusion; limited support for patients' organisations;…

41 *Knelpuntennota Zeldzame Aandoeningen, 2009, Vlaams Patiëntenplatform, http://www.vlaamspatientenplatform.be/www/component/option,com_docman/task,cat_view/gid,46/?mosmsg=You+are+trying+to+access+from+a+non-authorized+domain.+%28www.google.be%29*

42 *Website Rare Diseases Organisation Belgium, www.RaDiOrg.be*

43 *The Voice of 12,000 Patients: Experiences & Expectations of Rare Disease Patients on Diagnosis & Care in Europe, Results by Country, Belgium, 2009, Eurordis, http://archive.eurordis.org/IMG/pdf/voice_12000_patients/RARE_DISEASES_BELGIUM.pdf*

44 *Rare diseases and patients need, VPP, LUSS, RaDiOrg.be, oral presentation by Claude Sterckx and Lut De Baere.*

The diagnosis battle of Belgian patients[45]

- *Before obtaining the correct diagnosis, another diagnosis was given to 44% of Belgian patients with a rare disease resulting in inappropriate treatments in 75% of patients, including medical (36%), surgical (12%) and psychological or psychiatric (7%).*
- *For 78% of the Belgian rare disease patients, delays in diagnosis were considered responsible for at least one deleterious consequence, including death (1%); cognitive, psychological or physical problems, birth of another affected child, not adapted lifestyle and behaviour, lack of confidence in medicine.*
- *During the quest for diagnosis, 22% of Belgian rare disease patients consulted more than five physicians before receiving the correct diagnosis, 7% more than ten physicians.*
- *Diagnosis is expensive for Belgian patients and is rarely free (only 14% of diagnoses were free compared to 54% overall in Europe).*
- *A total of 22% of Belgian respondents obtained their diagnosis without receiving complete information on the disease. No psychological support was received by 60% of patients (which is low compared to 91% of respondents who expected this type of support but still represents the best value in the survey).*
- *The genetic nature of the disease was explained to families in 88% of cases, with details about the possibility of other cases in the family in 67% of cases. Genetic advice resulted in the diagnosis or identification of a carrier in the family in 36% of cases. A total of 30% of Belgian families considered the conditions of the announcement to be poor or unacceptable.*
- *In Europe 1 out of 4 patients with Ehlers Danlos syndrome waited for more than thirty years before being given the right diagnosis.*

The treatment need of Belgian patients

- *Belgian patients need an average of 9.5 different kinds of medical services related to their disease.*
- *Hospitalisation occurred in 47% of patients for an average total duration of 20 days in the last years.*
- *Access to eight services considered essential for each disease was easy in 77% of cases and difficult in 12% of cases and impossible in 11% of cases. This was mainly due to lack of referral (53%), unavailability (18%), personal cost (10%) and location of the structures, including a location too far away (13%), no one to go with (12%) and difficulty in travelling (15%).*
- *The medical services responded to patients' expectations fully (61%) or partially (27%), poorly (9%) or not at all (3%), which were comparable to overall results elsewhere in Europe.*

45 *The Voice of 12,000 Patients: Experiences & Expectations of Rare Disease Patients on Diagnosis & Care in Europe, Results by Country, Belgium, 2009, Eurordis, http://archive.eurordis.org/IMG/pdf/voice_12000_patients/RARE_DISEASES_BELGIUM.pdf*

The social needs of Belgian patients

Two patient platforms (VPP and LUSS) assessed the needs for patients with rare diseases, including their social needs and hidden costs.[46] Recently, Ms. Onkelinx, Minister of Social Affairs and Public Health conducted a similar inquiry for chronic diseases through their representative patients' organisations. Also Eurordis assessed the social services for patients with rare diseases in Belgium by surveying patients and their families. Information on the social services was gathered for eight different diseases with a total of 255 families having responded:

• Amongst the 48% of families that required social assistance, 1% failed to meet with a social worker, whereas 78 % met with one easily and 22% with difficulty.

• Compared to the European situation, this assistance was provided more frequently by associative and insurance structures, with 60% of Belgians being satisfied with this assistance and 16% not at all satisfied.

• As a consequence of the disease, 14% of Belgian patients had to move house. Amongst these, families most frequently moved to a more adapted house (58%), but also to be nearer to disease specialists (12%) or to be closer to a relative (19%).

• As a consequence of their disease, 36% of patients had to reduce or stop their professional activity. In 26% of cases one member of the family had to stop work to take care of a relative.

11 policy areas, 42 measures

2.17. This document contains a set of recommendations and measures in order to make up a comprehensive and integrated Belgian Plan for Rare Diseases.
The 42 proposed measures belong to the following 11 policy areas:

1. Improving the quality of diagnosis, therapy and patient management by setting up expert centres and expert networks
2. Codifying and inventorying rare diseases
3. Information and communication
4. Patient empowerment
5. Training and education of health professionals
6. Improving access to and financing of diagnosis
7. Improving access to and financing of treatment
8. Comprehensive care for the patient
9. Promoting research and transfer of research to diagnostics and treatment
10. Management of the Plan
11. Ethics and governance

46 *VPP Knelpuntennota Zeldzame Aandoeningen, http://www.vlaamspatientenplatform.be/www/component/option,com_docman/task,cat_view/gid,46/?mosmsg=You+are+trying+to+access+from+a+non-authorized+domain.+%28www.google.be%29 and LUSS Costs of chronic diseases.*

3. PROPOSED MEASURES BY ACTION DOMAIN

Area 1. Improving the quality of diagnosis, therapy and patient management by setting up expert centres and expert networks

Patient testimonials

"In 1994, my health deteriorated. The cardiologist who was treating me at the time delayed acting on it. He said that my cardiac valves had to be changed but at a later date when it became really necessary. My son, like myself, has tetralogy of Fallot and is treated in a specialised centre. I mentioned my problems to the paediatric cardiologist there who told me that I was being badly advised. He advised me to make an appointment with the adult cardiology department of his hospital. They operated on me rather quickly (but no valves). A few days later, I was back working at the factory."

"I have tetralogy of Fallot but I didn't realise that I could pass on this illness to my children. No doctor had ever told me that. My daughter was born 18 years ago without any health problems. During my wife's second pregnancy in 1998, after the ultrasound at six months, we were told that the baby had tetralogy of Fallot. We were really not expecting that."

"I watched my father, who had Huntington's disease, deteriorate every day. Yet neither my mother nor I received any information about the disease and we knew nothing about it. The neurologist just warned us that nothing could be done and that it would get worse and worse."

"For many years the doctors did not know what was wrong with me. They thought my problems and physical symptoms were all in the mind and that I should be admitted to a psychiatric ward. I spent ten years of my life in a psychiatric institution before people discovered that my condition has a name and I was not just imagining things. The diagnosis of Ehlers-Danlos syndrome got me out of psychiatric care and I am happy about that. I am only sad and angry about those ten lost years..." **47**

47 *Knelpuntennota zeldzame aandoeningen, Vlaams Patiëntenplatform, 2009, p.8, www.vlaamspatientenplatform.be/www/component/option,com_docman/task,cat_view/gid,46/Itemid,98/*

Introduction

1.1. After the appearance of the first symptoms, the confirmation of the diagnosis of a rare disease can sometimes last from 5 up to 30 years. This delay is common for patients with a rare disease and can bear dramatic consequences. Diagnosis is the basis for appropriate health care and of the possibility to get treatment. Several bottlenecks have been identified in the pathway leading to diagnosis of a rare disease, from the lack of recognition of symptoms by health care professionals to the limited availability of laboratory testing. It is therefore an area where appropriate health care policies can make real changes.

1.2. After the diagnosis, comes the fight to be heard, informed and directed towards competent medical bodies in order to get the most adequate treatment. For the vast majority of rare diseases, no protocol exists for good clinical practices. Where it does exist, the completeness of dissemination may not be optimal: not all health care professionals are always adequately trained, not all EU-countries have adopted and shared protocols. Additionally, the segmentation of medical specialities is a barrier to the multidisciplinary care needed by a patient suffering from a rare disease.

1.3. Although a number of patients with rare diseases may have the characteristics (e.g. severity, clinical complexity, genetic component,…) to benefit from the provisions by already existing health care services and policies, the lack of initiatives and health policies specifically targeted at rare diseases results in delayed diagnosis and difficult access to treatment and care.[48] The designation of expertise centres at national or regional level and their networking is an effective instrument for the provision of health care to rare disease patients. Designation of expertise centres allows the formal set up of a national framework of health care centres, which are acknowledged for their specific expertise in diagnosis and treatment of a specific rare disease or a group of rare diseases. They allow the process of definition of health care pathways, of collaboration and coordination for diagnosis and care, streamlining the patients to the most appropriate centres for their disease and enabling health care managers to identify where to allocate specific resources.[49]

1.4. Networking between expertise centres is an asset for quality care of rare diseases. The establishment of national and European networks of such centres should, according to Europlan, be considered a main priority for National Plans or Strategies. This networking, the sharing of information and reaching of consensus on the needs of these patients between experts, will play an important role in the further implementation of these proposals. This is also the case for the setting of priorities for research and the development of new treatments.

48 *Recommendations for the development of National Plans for Rare Diseases, Guidance document, EUROPLAN, p. 9, http://www.europlanproject.eu/public/contenuti/files/Guidance_Doc_EUROPLAN_20100601_final.pdf*

49 *Recommendations for the development of National Plans for Rare Diseases, Guidance document, EUROPLAN, p. 41, http://www.europlanproject.eu/public/contenuti/files/Guidance_Doc_EUROPLAN_20100601_final.pdf*

Measure 1.1. Creation of Centres of Expertise (CE)

Issue addressed:

1.1.1. In Belgium, the majority of patients with a rare disease do not have access to a dedicated centre, with recognised clinical expertise and up to date scientific knowledge on specific rare diseases or a group of rare diseases, and which can provide a multidisciplinary approach for diagnosis, medical and non-medical treatment and patient management. Only patients with cystic fibrosis, neuromuscular disorders and hereditary metabolic diseases have access to specialised centres, called reference centres. These centres have a contract (convention) with RIZIV/INAMI for reimbursement of certain treatment costs. Patients with a hereditary disease are usually referred to one of the 8 Belgian Centres for Human Genetics.

For some patients, it takes years before they are properly diagnosed, as their disease is not known to care providers because of its rarity, or because symptoms are not attributed to a rare disease.

Many patients are not treated to the current best standards, because their professional carers are not aware of the most recent treatment options because of the rarity of the disease of their patient.

Description of the measure:

1.1.2. **The establishment of a number of Centres of Expertise (CE) with expert clinical and scientific knowledge on a specific rare disease (e.g. cystic fibrosis) or on a group of rare diseases (e.g. neuromuscular diseases, metabolic diseases, genetic disorders)**.

The tasks for Centres of Expertise should be to:

- develop, apply and promote current best practice diagnostic techniques and medical and non-medical treatment, in accordance with best practices;
- conduct multidisciplinary consultations;
- initiate, monitor and adapt proper social (and financial) patient support through a 'care coordinator' (see also measure 8.1.);
- develop new clinical guidelines, in accordance and/or based (if possible) on international recognised and validated guidelines or good/best practices;
- register patients in the national registry (see also measures 2.1. and 2.2.);
- network with peripheral services (e.g. reporting to GPs, setting up of co-treatment schemes with peripheral specialists and peripheral hospitals, home care,…), with other expert centres (e.g. Centres of Expertise, Centres for Human Genetics, the Liaison Network for Rare Diseases (measures 1.2., 1.3),…) and with European and international expert centres (see also measures 1.4., 1.5., 1.6.);
- teach and train physicians and paramedical personnel (see also measure 5.1.);
- conduct scientific research (basic, translational, clinical) at international level (see also measures 9.1. - 9.5.);
- interact on a structural basis with rare disease patients' organisations and with the public at large (see also measures 3.1., 3.2., 3.3., 4.1., 4.2.);
- develop a system to monitor the activities at the CEs in order to be able to regularly report to the authorities who are responsible for the financing of the Centres of Expertise;
- contribute to exchanges and activities organised by the Platform of Rare Diseases (see also measure 10.1.);
- to provide clinical experts to participate in expert groups involved in the discussion of reimbursement criteria of orphan drugs (Colleges for Orphan Drugs (see § 2.11. and measure 7.9.)) or for the multi-stakeholder Working Committee (see measure 7.8.).

Note on the special case: rare cancers and subtypes of more current pathologies:

According to the members of the Fund, the proposed model of bringing together expertise in dedicated Centres which will apply a coordinated and multidisciplinary approach should work well for all rare diseases. It should be noted, however, that in the framework of other policy actions different models for the management of patients with a rare form of cancer are envisioned or being investigated. These include for example paediatric cancers (Initiative 12 of the Cancer Plan). Furthermore, the Belgian Health Care Knowledge Centre (KCE) will perform a study on the 'Organisation of care for rare tumours and tumours with complex treatment' (2011-024). The study has the intention to propose appropriate organisation forms for the treatment of rare cancers, on the basis of the Belgian situation and international experiences (see also initiative 13 of the Cancer Plan). Also the College for Oncology is working on a proposal on the matter. Furthermore, it is expected that patients with rare subtypes of more common diseases e.g. parkinson and other examples, will remain in the care of their specialist networks – in this case neurologists. On the other hand, these patients should benefit from the approved access to orphan drugs, developed for these diseases, and other drugs as proposed in the recommendations and proposals for measure for the Belgian Plan for Rare Diseases.

Expected impact:

1.1.3. Impact on patients

The creation of CEs has various impacts on the patients. The main impacts are at the level of diagnosis, treatment and patient support, resulting in an improved quality of life for patients and their relatives. Patient medical and non-medical care and social support is taking place in a multidisciplinary environment with medical, paramedical, psychological and social care expertise.

For patients with access to a CE, the delay in diagnosis should decrease as well as the rate of false diagnosis. Follow up in a CE should lead to better medical treatment (most adequate treatment, higher adherence rates,…), with decreased mortality and morbidity and longer (professional) life as a result.

The organisation of the care and patient management and the access to adequate social support will be facilitated and improved.

1.1.4. Impact on other stakeholders

General practitioners and local specialists will be able to easily identify the appropriate health care resources for their case. They will have structural access to expert opinions, and will get involved in the application of treatment plans and clinical pathways.

Policymakers will be able to better allocate financial resources. Furthermore, several studies, including studies from the Belgian KCE, have demonstrated that concentration of expertise for difficult conditions - like rare diseases - leads to better health care.

Aspects related to timing and implementation:

1.1.5. To become recognised, Belgian or foreign Centres of Expertise need to fulfil a number of criteria. Some of the criteria are considered essential; others are optional/informative or should be developed during future evaluation rounds. These criteria should ensure that recognised CEs truly apply a multidisciplinary approach and have high expertise on the rare diseases they are recognised for. The full list of proposed criteria for CEs is included in addendum 2 of this report.

1.1.6. This measure was already part of the Recommendations and Proposed Measures for a Belgian Plan for Rare Diseases – Phase I. On the basis of these recommendations and of a proposition of the Minister of Social Affairs and Public Health, a sum of 2,014 million Euro is foreseen in the 2011 RIZIV/INAMI budget for the setup of new Centres of Expertise. A working group will be established to further analyse the feasibility, the criteria and elaboration of this proposal.

1.1.7. Centres of Expertise should be re-evaluated on a regular basis (e.g. every five years).
At certain time points, new candidate centres can apply to become a Centre of Expertise. In principle, this can be for (groups of) rare diseases for which there are already existing Centres of Expertise, as well as for diseases which do not yet have such centres.

1.1.8. Current Reference Centres ('CF', 'metabolic', and 'neuromuscular') which are now operating on the basis of conventions (contracts) with RIZIV/INAMI, are expected, at some point in time, to become Centres of Expertise under the same recognition system as the newly established Centres of Expertise.
Some Centres for Human Genetics have European or even worldwide recognised expertise in the diagnosis and management of specific hereditary rare diseases. The Fund expects that these Centres will apply to become a CE for those diseases (see measure 1.2). Furthermore, the Centres for Human Genetics – which are funded with financial means which fall outside of the scope of the discussions in the working groups making recommendations and proposing measures for the Belgian Plan for Rare Diseases – constitute an important infrastructure and expertise which should be fully available to the CEs.

Aspects related to costs:

1.1.9. A conclusion from the experience with the conventions is that although the diseases are different, the average additional cost/patient/year is in a similar bracket (1.500 to 2.500 Euro/year). The convention pays for individual patients who receive regular treatment this sum (quarterly or annually). There is a threshold in number of patients (25 or 50), which means that if a centre does not reach the threshold, the convention does not pay for any patient.
This gives an indication of the cost to be expected in future of setting up more Centres of Expertise, except that the CEs could have supplementary tasks besides medical and paramedical treatment and coordination of treatment; they also could have a role in the setup, monitoring and adaptation of a patient specific roadmap for social and financial support, which is currently not in the task package of the reference centres. Therefore, the costs for the role of the care coordinators have to be added (see measure 8.1.).

1.1.10. If the measures proposed in this document are successfully implemented, one can expect up to 15.000 (additional) patients will have been diagnosed within a five-year period and will be treated annually in the network of Belgian CEs, leading to an additional yearly cost of up to 27 million Euro/year in the year 2016 (see chapter 5 and annex 8). This cost estimate is considering only the cost of multidiciplinarity and linked to the rarity of the disease and based on the experience with the reference centres that treat rare diseases. The actual cost will have to be defined for each individual disease based on an analysis of the economic consequences of the care path. They should be reassessed on a yearly base to be adapted to the changing care path.
As a comparison:

- the centres for Human Genetics are estimated to see in total some 10.000 patients/year for counselling. This number includes new patients, but also patients that were diagnosed in the past. It also includes family members. 80 % of rare disease patients are estimated to have a genetic disease.

- the networks of RIZIV/INAMI-conventioned reference centres (neuromuscular disorders, metabolic disorders, cystic fibrosis) are treating 3.500 to 4.000 patients/year.

More background on the budgetary aspects can be found in annex 8.

Measure 1.2. Consolidation of the role of the Centres for Human Genetics (CHG)

Issue addressed:

1.2.1. It is in the mission of the 8 Belgian Centres for Human Genetics to play an active and important role in the realisation of the European and Belgian measures concerning rare diseases. More than 80% of the rare diseases have a genetic basis while 90% of mono-genetically determined conditions are rare. Therefore the role of the Centres for Human Genetics in relation to the recommendations and proposed measures for a Belgian Plan for Rare Diseases should further be clarified.

1.2.2. The Centres for Human Genetics are represented by the High Council for Anthropogenetics, which will be transformed into a College for Genetics. At the time of writing of these proposals for a Belgian Plan for Rare Diseases, the Centres for Human Genetics were negotiating with RIZIV/INAMI a convention for covering the costs for genetic counselling in an appropriate medical and paramedical approach in the framework of the Cancer Plan. These conventions also include guarantees for adequate quality control and registration of clinical activities.

Description of the measure:

1.2.3. **It is expected that the network of Centres for Human Genetics consolidates its role in the management of patients with a rare disease**.

The members of the Fund for Rare Diseases and Orphan Drugs explicitly recognise that the Centres for Human Genetics currently:

- have a broad medical and multidisciplinary expertise on inherited diseases, (which form a large part of rare diseases);
- dispose over state of the art technical DNA and other testing facilities for diagnosis;
- organise a high quality patient and family oriented genetic counselling;
- have a patient oriented medical network with 'organ specific' specialists, general practitioners and paramedical professionals;
- perform a wide variety of (internationally recognised) research activities on rare genetic diseases;
- have intensive contacts with patients organisations;
- participate in international networks.

All these activities should at least be continued, and preferably intensified. They should remain an important entry point for new patients with a rare disease (and for a number of patients even the most most important one) into an anticipated system of expertise for treatment and patient management.

1.2.4. Furthermore, Centres for Human Genetics are expected, in the framework of a future Belgian Plan for Rare Diseases to:

- apply to become Centres of Expertise for those rare diseases or groups of rare diseases for which they have recognised expertise (possibly in partnership with other medical experts at their hospitals);
- register their patients in the National Registry for Rare Diseases which will be hosted at the Scientific Institute of Public Health (measures 2.1. and 2.2.);
- create and/or reinforce functional networks with the existing conventioned Reference Centres and the newly started Centres of Expertise (measure 1.1) and the Liaison network for Rare Diseases (measure 1.3.) at their hospitals and in their region;
- coordinate and adjust activities within the network of Centres for Human Genetics to increase expertise, be able to keep updated on new technologies, avoid unnecessary duplication;
- manage coordinated criteria on the clinical utility of tests. The centres play a gate keeping role and this role should be based on criteria that are common to all centres and be transparent;
- define and implement quality indicators, seek accreditation of their laboratories for diagnostics and clinical activities (if these are not already applied);
- develop initiatives to raise their visibility and intensify contacts with patients' organisations;
- develop effective initiatives and mechanisms to decrease the long time to diagnosis for rare disease patients, complementary to what is described in § 1.3.

Expected impact:

Impact on patients

1.2.5. For many patients with a rare disease the Centres for Human Genetics form already an indispensible cornerstone for their diagnosis and disease management. By the commitment from the Centres for Human Genetics to continue and further strengthen their role, to reinforce functional networks with other medical experts and to keep on conducting research in the area of rare diseases, patients are guaranteed to have accessible entry to multidisciplinary and diagnostic expertise, genetic consult, and up to date disease management.

The measures proposed are expected to lead to:

- savings as a result of better coordination and specialisation of the Centres;
- better quality of service, as centres will all have certified quality management systems;
- better quality for money and equity, through a coordinated and transparent approach with regard to the clinical utility of tests.

Aspects related to timing and implementation and aspects related to costs:

1.2.6. During the development of the proposals for a Belgian Plan for Rare Diseases, the High Council for Anthropogenetics, the FPS Health Care and the RIZIV/INAMI were in the process of redefining the role and the financing mechanisms for the Centres for Human Genetics. These negotiations fall outside of the scope of the activities of the working groups and the Fund for Rare Diseases and Orphan Drugs, and thus of the recommendations proposed in this document.

Nevertheless, some Centres for Human Genetics are expected to become themselves Centre of Expertise for specific rare diseases. The additional costs this will generate for them, would be covered through measure 1.1 and therefore does not appear under this measure 1.2.

1.2.7. Still, a specific budget is proposed for measure 1.2. to cover (part of) the investment costs the Centres for Human Genetics need to make for developing quality management systems and becoming certified. Quality management is one of the necessary investments to ensure the CHGs can take up their role in the network and in an EU context. The budget proposed is a fund of 400.000 Euro that would be made available to the centres to fund investment costs (see annex 8).

1.2.7. Furthermore, the provision for a budget for DNA-tests performed abroad (see measure 6.1.) is foreseen in the context of these proposals. This budget will be mainly allocated to the Centres for Human Genetics through a convention (contract) with RIZIV/INAMI.

More background on the budgetary aspects is included in annex 8.

Measure 1.3. Creation of a Liaison network for Rare Diseases (LRD)

Issue addressed:

1.3.1. The existence of a number of Centres of Expertise for specific rare diseases or groups of rare diseases, and of the Centres for Human Genetics, will in itself not fully resolve the problem of delay in diagnosis and lack of proper patient management for a certain group of rare disease patients, especially those patients with an ultra-rare disease, patients with a disease for which there is no Centre of Expertise, and patients who have to go to a Centre of Expertise outside of Belgium and who need extra follow up and support from a centre within Belgium. For those patients, a supplementary network with a number of specific tasks needs to be set up.

Description of the measure:

1.3.2. **The establishment of a network of diagnostic and treatment units for rare disease patients (Liaison network for Rare Diseases or LRD) which perform a multidisciplinary rare disease consultation (MRDC)**. The network should accept any patient with a presumed or unknown diagnosis for which there is some suspicion that the patient has a rare disease. The multidisciplinary team linked to the local unit of the LRD offers a multidisciplinary and integrated evaluation of the patient's medical condition. The Liaison Centres for Rare Diseases will de facto be located in larger hospitals – most probably University Hospitals – and form a network of expertise.

1.3.3. The Liaison network is intended for:

- the diagnosis of patients which have not been diagnosed in a Centre of Expertise or a Centre for Human Genetics. Once a diagnosis is definite, the patient should be referred to an appropriate Centre of Expertise, if available;
- the follow up of patients who do not get a final diagnosis;
- the follow up of patients with a rare disease for whom there is no recognized Centre of Expertise;
- the follow up of patients who are treated in a Centre of Expertise outside of Belgium and who are not followed adequately in a Centre of Expertise in Belgium.

1.3.4. The concrete tasks of the individual centres forming the network are to:

- organise a 'multidisciplinary rare disease consultation'-clinic (MRDC) with joint staff meetings;
- develop procedures for multidisciplinary consultations in accordance with international standards and guidelines;

- organise the follow up of patients with a rare disease for whom there is no expert treatment available in Belgium;
- register patients in the national register (see also measures 2.1. and 2.2.);
- form a functional network with the Centres of Expertise and the Centre for Human Genetics within their own hospital, including agreements and procedures on responsibilities, tasks, and collaboration;
- collaborate with other LRD-units at other hospitals;
- network with peripheral services (e.g. reporting to GPs, setting up of co-treatment schemes with peripheral specialists and peripheral hospitals, home care,…)(see also measure 1.5.), with other expert centres (e.g. Centres of Expertise, Centres for Human Genetics,…) and with European expert centres (see measures 1.5. and 1.6.);
- teach and train physicians and paramedical personnel (see also measure 5.1.);
- conduct scientific research (basic, translational, clinical) at international level (see also measures 9.1.- 9.6.);
- develop a system to monitor the activities of the network in order to be able to regularly report to the authorities who are responsible for the financing of the network;
- contribute to exchanges and activities organised by the Platform of Rare Diseases (see also measure 10.1.);
- interact on a structural basis with rare disease patients' organisations and with the public at large (see also measure 3.1., 3.2., 3.3., 4.1., 4.2.);
- to provide clinical experts to participate in expert groups involved in the discussion of reimbursement criteria for orphan drugs (Colleges for Orphan Drugs (see 2.11. and measure 7.9.) or the multi-stakeholder Working Committee (see measure 7.8.).

1.3.5. The individual centres forming the Liaison network for Rare Diseases

- will, probably de facto, be hosted in university hospitals (see list of criteria for recognition in annex 2) and would work in close cooperation with the CEs hosted inside these hospitals;
- are operating as a network;
- need to create a strong link with the "care coordination" function as described in measure 8.1;
- are headed by a Liaison Officer who is responsible for the operation of the centre, but who is also the link between the Platform, the University Hospital and the authorities on matters related to rare diseases. This responsibility implies the monitoring of all rare disease activities inside the hospital with particular attention to the multidisciplinary nature of the care and the constructive cooperation between teams and institutions for the benefit of the patient. The Liaison Officer is expected to become 'Mr or Ms Rare Disease' inside the hospital, and as a group, the Liaison Officers are expected to become an operational network team that can help to implement and operationalize the future Belgian Plan for Rare Diseases.

Expected impact:

1.3.6. Impact on patients

It is expected that for patients with rare diseases the main gateway to get initial access to expert diagnosis, treatment and patient management will be at the level of the Centres of Expertise and the Centres for Human Genetics. But for those patients who slip through the net because their disease is 'unknown' or because they cannot be helped in one of the Centres, the Liaison network provides an essential and necessary solution.

The first impact of the network is the easier access to diagnosis: the Liaison network should become like a brand name, THE place to send a patient that proves difficult to diagnose. The impact of the network is at the level of the integrated and multidisciplinary diagnosis. Secondly, the network centres are expected to refer these diagnosed patients to Centres of Expertise for expert treatment and patient management. For those patients who cannot be diagnosed, who do not have access to expert treatment in Belgium or who go to a CE

abroad, proper patient management should be ensured at the network centre level.
Follow up in a Liaison centre lead to better medical treatment (more adequate treatment, higher adherence rates,…), with decreased mortality and morbidity and longer (professional) life as a result.
Patients are guided towards adequate social and financial support, also for patients who are treated in a Centre of Expertise outside of Belgium.
All interventions at the level of the Liaison network should improve quality of life for patients and their relatives.

1.3.7. Impact on other stakeholders
General practitioners and local specialists will be able to identify the appropriate health care resource for their case. They will have structural access to expert opinions, and will get involved in the application of treatment plans and clinical pathways (see also measure 1.5 and 8.1).
Policymakers will be able to better allocate financial resources.
The Liaison Officers will contribute to the activities of the proposed Platform for Rare Diseases, and therefore each University Hospital with a Liaison centre will have a direct contact point with the Platform.

Aspects related to timing and implementation:
1.3.8. To become recognised, the Liaison centres need to fulfil a number of criteria. Some of the criteria are considered essential, others are optional/informative or should be developed in the future. These criteria should ensure that recognised network centres truly apply a multidisciplinary approach and have sufficient expertise. The full list of criteria for centres forming the Liaison network for Rare Diseases is included in addendum 3 of this report.

1.3.9. Centres forming the Liaison network for Rare Diseases should be re-evaluated on a regular basis (e.g. every five years).

Aspects related to costs:
1.3.10. The financing of the Liaison network for Rare Diseases has two components: one is linked to each individual patient, the second is linked to the role of the Liaison Officer and is a fixed cost.

1.3.11. For the first component the Multi-Disciplinary Oncological Consultation (MOC) is a possible existing financing model for the organisation of the multidisciplinary rare disease consultation. The MOC is reimbursed separately to ensure consensus building among various disciplines before decision-making on an individual patient treatment. A similar approach could be used for the multidisciplinary rare disease consultation (MRDC). Such an approach would ensure that the additional costs carried by centres due to the multi-disciplinary nature of the rare diseases are covered. It would however not cover the costs of paramedical and non-medical staff. Assuming that the Multidisciplinary Rare Disease Consultation (MRDC) would be reimbursed at 250 Euro on top of the nomenclature reimbursement for the medical acts and tests, and assuming that all centres belonging to the Liaison network would in aggregated yearly see approximately 2.000 patients, the total cost of this measure is estimated at 500.000 Euro/year (see annex 8).

1.3.12. The second component would be to finance the salary for the Liaison Officers. The budget impact is estimated at one halftime post at senior medical level for each University Hospital. The total cost is estimated at 500.000 Euro/year (see annex 8).

1.3.13. On top of this, the Liaison centres are expected to coordinate the care of (part of the)patients that were sent to CEs in other EU countries. This is expected to be a percentage of the patients that are treated in national CEs, e.g. 20% of 15.000 after 5 years of implementation of the Belgian Plan for Rare Diseases. The costs for this function are covered by measure 8.1 and measure 1.1.

More background on the budgetary aspects are included in annex 8.

Measure 1.4. Networking between Centres at national level

Issue addressed:

1.4.1. Networking between Centres of Expertise, Centres for Human Genetics and the Liaison network for Rare Diseases is an asset for quality care of rare diseases. Patients with a rare disease will get better treatment if good practice diagnostic techniques and good practice therapeutic approaches are shared between all Centres.
Centres should therefore collaborate intensively and not operate in a modus of mutual competition.
Because of the current fragmentation of the supply of care, Belgian patients miss opportunities to participate in clinical trials.

Description of the measure:

1.4.2. Networking at national level between Centres should be considered at two levels: networking between CEs for the same disease or group of diseases, and networking between all recognised CE, CHG and the LRD.

1.4.3. For the first level, the following recommendation is made:
All certified CEs for the same specific disease or for a group of diseases are expected to take part in the development of guidelines, of clinical pathways, and the set up and maintenance of a disease specific registry soon after the Centres are being recognised (see criteria list for CEs in addendum 2). This will ask a number of meetings between representatives of the CEs. These meetings mark the beginning of their formal networking.

After this initial phase, all disease specific CEs are expected to meet formally at least once a year in order to:
- exchange good practices on diagnosis, medical and paramedical treatment and aspects of social care;
- set up cooperation on fundamental, clinical and translational research;
- actualize guidelines and clinical pathways according to international standards and linked with international initiatives;
- review status of disease specific registries;
- harmonize quality of care;
- work out parameters and evaluation schemes for quality control.

If necessary, experts from other institutes/organisations should be involved in this process.

The proposed Platform (measure 10.1.) could, in collaboration with the competent authorities and organisations responsible for the implementation and financing of the Centres of Expertise, be an efficient structure to organise and streamline this process in collaboration with other parties (i.e. Colleges, KCE,…).

1.4.4. **For the networking between all CEs, CHGs and the LRD, the recommendation is made to organize yearly a symposium/general network meeting with representatives from all Centres. This meeting could be organized by the Platform in collaboration with the competent authorities and organisations responsible for the implementation and financing of the Centres**.

Expected impact:

1.4.5. Active and regular information exchange will increase the expertise of all experts involved.
This will lead to faster implementation of innovative diagnostic techniques and treatment approaches, which will benefit the patients.
Through networking Belgian CE's will increase their research potential, both on fundamental, translational and clinical research, including the participation in clinical trials.

Aspects related to timing and implementation:

1.4.6. Centres of Expertise are expected to have their first formal network meeting within 3 months after their recognition. The first national network meeting between all CE's will take place in the second year after the establishment of the Platform for Rare Diseases.

Aspects related to costs:

1.4.7. No additional costs are expected at the level of the CEs. Costs for organising meetings and network meetings are at the level of the Platform (see measure 10.1.) and are budgeted at 50.000 Euro per year (see annex 8).

Measure 1.5. Networking between Centres and peripheral care services

Issue addressed:

1.5.1. CEs, CHGs and LRD should have a complementary role vis-à-vis local medical (general practitioners, specialists, regional hospitals,…), paramedical (physiotherapist, speech therapist,…), psychological and other care services.
Expert centres should work out optimal and updated individualised treatment schemes for each patient based on best clinical practice. For day-to-day follow up and treatment of the patients they should operate on the basis of 'shared care' principles with local services. The CE or LRD centres have the role of 'coordinator' and should ensure that, in the interest of the patient, each treatment act is performed at the most appropriate service level (home care, first, second, third or fourth (CE or LRD) line of care)
It should be avoided that patients need to travel long distances to CEs for treatments which can be administered at local level as well.

Description of the measure:

1.5.2. **Centres of Expertise, Centres for Human Genetics and LRD centres should set up networks with peripheral care services**, i.e. with:
the general practitioner (GP) of the patient.

- After every patient contact at a Centre, the GP should receive a report from the Centre with the following information:
  - ◇ condition of the patient;
  - ◇ treatment plan and patient management plan (eventual changes);

  - ◇ tests/referrals which have been planned;
  - ◇ how to act in case of emergency;
  - ◇ contact point at the Centre (including mobile phone number of responsible/coordinating physician at the Centre).
- GPs should get electronic access to the patient records at the Centre. If currently not yet possible, Centres should make efforts to make this service available in the future.
- GPs should be allowed to take part in the multidisciplinary consultation/deliberation at the Centre if they and the patient request this.
- GPs should be involved in the day-to-day follow up of the patient.

peripheral specialists and hospitals
- The Centre should propose to the treating peripheral specialists and hospitals a shared follow-up procedure for each patient (if the peripheral medical service is open to this).
- Treating peripheral specialists should get electronic access to the patient records at the Centre. Centres should make efforts to make this service available in the future, if this is not the case at the moment.
- Treating peripheral specialists should be allowed to take part in the multidisciplinary consultation/deliberation at the Centre if they and the patient request this.

local paramedical services
- Centres should provide individual treatment plans for local paramedical services, preferably in collaboration with local treating specialist and/or GP.

local social services
- The care coordinator in the Centre should contact the local social services, if necessary (see measure 8.1.).

pharmacists
- local pharmacists should be motivated to follow the detailed procedures for preparation of medicines as described on the website of the 'Therapeutic Magistral Formularium' (*www.vza.be*); should take the responsibility of the pharmaceutical care: prevention, information, referral and adherence.

patient organizations
- Centres are obliged to network with patient organizations (see list of criteria). This collaboration should have a number of formal aspects (see measure 4.2. in the area 'patient empowerment') and informal aspects (participation to patient organization days, giving disease and disease management related information etc.…).

Expected impact:

1.5.3. Patients will be treated, in their own interest, at the most appropriate care service level (home care, first, second, third or fourth (CE, CHG, LRD) line of care. Supervision of treatment lies at the Centre, so expert treatment remains guaranteed.

Fluent information sharing and the making of clear arrangements between the different care levels will increase the chances that the patient receives optimal, integrated, individually adapted and patient centred care. Also the adherence of the patient to the treatment will increase.

1.5.4. Networking, communication and information sharing between Centres and peripheral carers will increase the expertise of peripheral services and raise the awareness of these services towards rare diseases.

Aspects related to timing and implementation:

1.5.5. Centres are encouraged to set up networks with peripheral services immediately after they have been recognised.

Aspects related to costs:

1.5.6. Networking with peripheral care services are part of the normal task package for which Centres receive funding through measure 8.1. Nevertheless a budget will be foreseen for this proposal, specific for the development of a software instrument to increase the efficiency of the communication between the different care providers and the different care levels (national/international; first/other lines; centralised/peripheral). The foreseen investment budget is set at 250.000 Euro.

More background on budgetary aspects is included in annex 8.

Measure 1.6. Networking at European and international level.

Issue addressed:

1.6.1. In order to guarantee that patients with a rare disease in small countries, like Belgium, get access to a Centre of Expertise, bilateral, cross-border and European cooperation will be necessary. This issue is also on the agenda of the EU Commission, Council and Parliament.[50]

Networking of Belgian Centres of Expertise, Centres for Human Genetics and centres belonging to the Liaison network, with European and international 'sister organisations' will increase the level of expertise at Belgian level and opens opportunities for research.

According to Orphanet, researchers and clinicians located in Belgium are participating/have participated already in 79 'European or international networks'. This means coordinated activities with financing and/or an official designation by a European official body (DGSanco, E-Rare Consortium, DG Research (FP5, FP6, FP7)).[51]

Description of the measure:

1.6.2. The promotion of European networking can be divided in three main sub-measures:

Measure 1.6.a. Belgian authorities should be able to recognise Centres of Expertise outside of Belgium for (ultra)-rare diseases for which there is insufficient expertise in Belgium.

Measure 1.6.b. The Belgian representative at EUCERD and at other relevant organisations should take a leading role in the promotion and setting up of appropriate European policy frameworks to allow collaboration agreements between countries.

50 *Cross-border care, European Commission, Public Health, http://ec.europa.eu/health/cross_border_care/policy/index_en.htm and Directive of the European Parliament and of the Council on the application of patients' rights in Cross-border healthcare, http://register.consilium.europa.eu/pdf/en/11/pe00/pe00006.en11.pdf*

51 *European collaborative research projects funded by DG Research and by E-Rare in the field of rare diseases & European clinical networks funded by DG Sanco and contributing to clinical research in the field of rare diseases, Orphanet Report Series, Rare Diseases collection, January 2011, http://www.orpha.net/orphacom/cahiers/docs/GB/Networks.pdf*

Measure 1.6.c. Each Belgian CE should take (active) part in European and international networks of expert centres for the disease(s) they are recognised for. Furthermore, a CE has to conduct research in the diseases it is considered expert in (see criteria list in addendum 2).

This criterion already forms (to some extent) a guarantee that the CEs are involved in international networking. Nevertheless each CE has to document and objectify this. If a CE is not involved in an international network, one can expect that it will connect to one or more international networks in due course. International networking can consist of and should be evaluated on the basis of three aspects:

- attend and participate actively (in the form of poster or oral presentations) in international conferences regarding the disease or group of diseases one is recognized for;
- be registered in a relevant international network of expert centres;
- publish in peer reviewed journals on the disease or group of diseases one is recognized for.

Expected impact:

1.6.3. Increase the access of Belgian patients with a rare disease to expert treatment.
Active and regular information exchange at international level will increase the expertise of all experts involved. This will lead to faster implementation of innovative diagnostic techniques and treatment approaches, which will be beneficial to patients.

1.6.4. Through international networking Belgian CEs will not only increase their expertise but also their research potential, both on fundamental, translational and clinical research, including the participation in clinical trials.

Aspects related to timing and implementation:

1.6.5. Setting up the proper frameworks at EU level to allow patients with a rare disease to travel to foreign Centres of Expertise in order to receive expert and reimbursed treatment, falls under the broader scope of cross border health care, an issue which is currently being discussed at EU level.
Measure 1.6.b. proposes not to wait until an EU consensus is reached on this topic, but to stimulate the recognition of cross border expertise at bilateral level as soon as possible.
Furthermore, Centres of Expertise are encouraged to participate in international networks before or immediately after they have been recognised.

Aspects related to costs:

1.6.6. A budget of 50.000 Euro per year is proposed for this measure. The follow up and the support of this networking process can be managed at the level of the proposed Platform for Rare Diseases (measure 10.1) in collaboration with the authorities responsible for the financing of the Centres and the authorities involved in the negotiations at European and international level.

More background on the budgetary aspects is included in annex 8.

Area 2. Codifying and inventorying rare diseases

Patient testimony

"In August 2006, we learned that a clinical trial was about to start for the illness our daughter has. Her two regular doctors had heard nothing about it. A neurologist who was also a researcher at the FNRS (National Fund for Scientific Research in Belgium) supported us. He contacted the Parisian doctor in charge of the study. Our health insurers refused to cover the hospital costs in Paris but this researcher defended our case and we received cover."

Introduction

2.1. The available epidemiological data on most rare diseases are inadequate to give firm details on the number of patients with a specific rare disease. In general, people with a rare disease are not registered in databases.

2.2. One of the main problems in planning health care for rare diseases is that the burden of most of them is invisible to the health systems, due to misclassification and the lack of registration and appropriate coding. Many rare diseases are summed up as 'other endocrine and metabolic disorders'. As a consequence it is difficult to register and calculate the costs involved in rare diseases on a national or international basis, and in a reliable, harmonised way.[52]
For this reason, codification is a central topic in the European initiatives on rare diseases. Specific actions have been taken in the past years by the Rare Disease Task Force (RDTF) leading to the creation of a working group for the classification of rare diseases in conjunction with the World Health Organisation (WHO). This working group operates in the framework of the revision of the International Classification of Diseases (ICD), which has been launched by the WHO in 2007.

2.3. Disease-specific registries or registries for groups of rare diseases are an effective way to assess health care needs as well as to generate research in several areas, including epidemiology since these registries are often the only existing source of scientific/clinical and epidemiologic information on rare diseases. Today, almost all registries are academic, usually established by clinicians interested in a particular disease or group of diseases. They have to face the difficulties of long-term sustainability, personal data protection and patient sample representativeness. While current registries represent an opportunity of getting high quality information, a systematic approach to registration is necessary to exploit this opportunity and substantially improve the information on rare diseases. The added value of registries has been extensively assessed and established in the past years from the work of the RDTF and was strongly supported in the Recommendations by the European Council.

2.4. An important issue to be addressed is the protection of personal data, which is of very high relevance if databases/registries with personal data are to become a popular tool for the collection of information and of knowledge improvement on rare diseases.
At the same time, as companies have to set up product-specific registries at the request of the EMA or from the national reimbursement authorities for many orphan drugs, there may be multiple registries for the same rare

52 *Background paper on orphan diseases for the WHO Report on Priority Medicines for Europe and the World, October 2004.*

disease if multiple treatments are approved. The demands to the Colleges for orphan drugs can also be seen as a registry. Ideally, one should strive for a single disease register with different access for different parties (authorities, physicians, companies) according to their needs. This will motivate the prescribers to do a good job, and ameliorate the quality of the registration. However, the transition from the current system of product registries to disease registries should be studied well in terms of regulatory requirements at EU and national level, quality, financing and privacy protection. Belgium should take a leading role in discussion this at EU level.

Measure 2.1. Creation of a national Belgian Registry for Rare Diseases

Issue addressed:

2.1.1. In order to make epidemiologic surveillance of rare diseases possible, a centralised registry at national level, including the planned register for genetic diseases, should be created, supported and funded. The main aim of this registry is to provide an indication of the number of people suffering from a specific rare disease in Belgium, to provide information about the providers of treatment of the patient and the management of his needs and rights. The registry should be able to trace back the patients through the registering physician in case of new fundamental research, trials or therapies.

Description of the measure:

2.1.2. **Already in the Recommendations and proposed measures for a Belgian Plan for Rare Diseases - Phase I, the recommendation was made to create a National Registry for Rare Diseases**. In the proposal it was suggested that the centralised registry would at least contain the following variables: Unique code of the patient (generated by registry), Gender, Age at 31dec, Unique code of registering physician (riziv nr), Unique code of the expert centre (riziv nr), Unique identification number of the rare disease, Age of onset of symptoms (national plan indicator), Age of diagnosis, Postcode of residence, Means of diagnosis confirmation (genetic, biochemical, histological), Additional social allowances, Working regime (student, no work, part time, full time), (Eventual) Date of death, Link to disease specific registries (if applicable).

2.1.3. Patients should be registered at time of diagnosis by a recognised Centre of Expertise. Further entries should take place at time of death and updated at regular intervals in between (at least every 2 years). The registration procedure should be web based and will be worked out in collaboration with eHealth.

2.1.4. Patients have to give informed consent for registration. Registration of patients is an obligatory criterion for recognition and financing for the Centers of Expertise. The database structure, access and content, the informed consent procedure, the registration protocols and study procedures will be conform the Belgian and European legislation on privacy issues.

2.1.5. In the database diseases will be coded and classified according to the (future) 11th revision of the International Classification of Diseases (ICD11).[53] Representatives of the European Rare Diseases Task Force are, in conjunction with the World Health Organization (WHO), working on a revision of the classification of rare diseases in the framework of ICD11. In the mean time, the list of rare diseases published by Orphanet could be used as a reference, since it is the most comprehensive list developed today, regularly updated and it forms the basis for the future ICD11 chapters on rare diseases.

53 *Revision of the Internal Classification of Diseases, World Health Organisation, http://www.who.int/classifications/icd/ICDRevision/en/*

2.1.6. The Belgian registry should be part of existing global registries (EuroCAT, and others) and should be able to connect to and exchange information with other relevant European and international databases. Therefore, the management of the registry should seek collaboration with partners from other EU Member States and with relevant European organisations in order to increase accessibility, applicability and usage of the data, providing that the appropriate access keys and procedures to guarantee privacy are put in place and agreed upon at EU level.

Expected impact:

2.1.7. Impact on patients

Through the registry patients remain traceable and will no longer 'get lost' in the system. This increases their chances for regular follow up at Centres of Expertise and for participation in scientific research, including clinical trials. Furthermore, the registry might one day become a tool to improve adherence to therapy, and access to therapy.

2.1.8. Impact on other stakeholders

Registries are important tools for research, i.e. it allows researchers to follow up the natural course of the disease and registries are indispensable for translational research and clinical trials.

For policymakers epidemiological data on rare diseases will become available, allowing better planning of appropriate health and social care for patients, administrative processes and procedures can be simplified and registries could eventually deliver the necessary data for post-marketing surveillance (pharmacovigilance, clinical benefit,…) of orphan drugs, medical devices and other treatments options.

For companies, registries might provide easier access to patients in the organisation of clinical trials, and will also help them to set priorities in R&D, as well as potentially provide data on product improvement at the time disease registries are also added in.

Aspects related to timing and implementation:

2.1.9. The proposal for the setup of the centralised National Registry for Rare Diseases was already part of proposals formulated during Phase 1. On the basis of these proposals and of a proposition by the Minister of Social Affairs and Public Health a sum of 200.000 Euro is foreseen in the 2011 RIZIV/INAMI budget supporting a new initiative to create a National Registry for Rare Dsieases.

The IPH/WIV has been commissioned by the Minister to make a proposal for creating and hosting the Registry in collaboration with other instances such as RIZIV/INAMI, FOD/SPF,…. The IPH/WIV has already experience in hosting the Belgian Cystic Fibrosis Registry (Belgisch Mucoviscidose Register - Registre Belge de la Mucoviscidose - BMR-RBM) and the Registry for Neuromuscular Disorders. Both registries have already been approved by several committees, interfaces have been tested and connection with eHealth has been created.

Aspects related to costs:

2.1.10. An investment and operating budget of 200.000 Euro for a new initiative to create a National Registry for Rare Diseases was already foreseen in the 2011 RIZIV/INAMI budget.

2.1.11. The proposal of the Fund is to earmark two different budgets from 2012 onwards: a yearly budget to cover the running costs of the registries and a budget to cover development costs, essentially to integrate existing disease registries, develop new ones (measure 2.2) and integrate the registry into an (international) e-care platform.

Both budgets should be used in the most efficient way, through EU level cooperation, to increase the number

of diseases and patients included in the system. The foreseen total budget (including Phase I) for the development of the registry over a period of 5 years is estimated at 2 million Euro.
The foreseen total budget (including Phase I) for running the registry over the same period is 1,250 million Euro.

More background on the budgetary aspects is included in annex 8.

Measure 2.2. Creation and/or validation of disease or group of diseases specific sub-registries linked to the Belgian Registry for Rare Diseases

Issue addressed:
2.2.1. As indicated earlier, disease-specific registries or registries for groups of rare diseases are an effective way to assess health care needs as well as to generate research in several areas and to induce networking between scientists, medical experts and Centres of Expertise. Disease or disease group specific registries are important for collecting epidemiological, medical and social data for as many patients as possible; for describing and evaluating care in the Centres of Expertise; for providing a database to be used in clinical, basic and epidemiological research; and to participate to European or international research projects (fundamental, translational, clinical), registries and surveillance programs.

Description of the measure:
2.2.2. **The National Belgian Registry for Rare Diseases will provide a stable environment for the 'plug&play' implementation of extra disease specific registries (new or existing ones) or temporary trial questionnaires.**

These disease specific registries may be set up by IPH/WIV in collaboration with the Centres of Expertise recognised for that specific disease or group of diseases, with relevant patient organisations and with representatives from relevant administrative and governmental bodies as well as from industry, or at EU or international level together with similar bodies in other countries.
The disease specific variables should at least constitute a minimal set of parameters mirroring the minimal set proposed by the EpiRare European project.
The disease or disease group specific registries should be able to connect to other similar registries in other EU countries and to medicinal product specific registries, if appropriate. Therefore, the coordinators of the disease specific registries and the IPH/WIV registry team should collaborate with all relevant (European) stakeholders.

Expected impact:
2.2.3. The expected impacts of disease or disease group specific registries is similar to the ones described under measure 2.1.

Aspects related to timing and implementation:
2.2.4. Several rare disease specific registries have been developed in the national Belgian context or the European context. Other registries need to be built from the start. It is expected that the IPH/WIV registry team would start with the implementation of these disease specific registries from the moment the central registry is up and running. A plan to move from the current product-based registries to disease registries should be carefully discussed and planned at EU level.

Aspects related to costs:

2.2.5. The budget estimation for this area has already been described under measure 2.1 (see also Tables 1 and 2 in Chapter 5).

With this budgetary set-up, the number of new diseases covered is expected to be relative low at the start of the Plan (5-6 diseases in first year), but much higher in the fifth year of implementation.

More background on the budgetary aspects are included in annex 8.

Area 3. Information and communication

Patient testimonials

"Nobody told us about the on-going administration that we had to do. You have to find out about these things yourself. I was not even informed that M. (who has leukodystrophy) no longer had 'serious illness' status. It was the physiotherapist who noticed it and reminded me to restart the process. When dealing with such an illness, you have to be very resourceful and constantly be looking for useful information yourself. If you don't, you will get nowhere. I have just found out that there is an exhibition on disability which nobody had ever told me about. I wonder how parents manage if they are suffering from exhaustion or if they are not clued in."

"The neuropaediatrician explained to the physiotherapist that he knew the young girl's (known as M.) diagnosis although he was not 100% sure. It was leukodystrophy but he said not to say anything to the parents because he was worried about how they would react. He later explained that he had previously informed parents about such a thing and they seemed to give in and not give all the necessary care. He also feared that the parents would resort to the Internet to read up on the details of the disease."

Introduction

3.1. Patients with rare diseases and their families experience major difficulties in getting information on their disease (especially in their own language and adapted to their questions and needs) and finding their way within the health care system. Patients are faced with a lack of information on the clinical features caused by their disease, on measures for social and economic assistance, and on the location of the centres providing appropriate expertise and care, and on the activities they can carry out to alleviate the burden of the disease in everyday life. The provision of accurate information in a format adapted to the needs of patients and their families is an important instrument to cope with the day to day discomfort caused by the disease.

3.2. Similarly, health care professionals facing rare diseases do not have easy access to information, and available information is scattered and scarce, with lack of guidelines and validated evidence.

3.3. Disease-specific websites about patients' associations, networks of reference, registries or specific activities on rare diseases are very important sources of information frequently used by patients. Websites and other information tools at national level, which provide global information on rare diseases, are going to be more effective when, in addition to specific information on national and regional initiatives, they contain links to international information portals and institutions to facilitate access to additional information resources, such as the section on rare diseases of the EU Public Health website, the EMA website, and ORPHANET and any other relevant website for rare diseases.[54]

54 *Recommendations for the development of National Plans for Rare Diseases, Guidance document, EUROPLAN, p. 61, http://www.europlanproject.eu/public/contenuti/files/Guidance_Doc_EUROPLAN_20100601_final.pdf*

3.4. Finally, the increase of the awareness on rare diseases in the general public should be considered. Different activities, such as further promotion of Rare Disease Day and other events which could raise awareness deserve further support.

Measure 3.1. Creation of a national portal website with actual and validated information

Issue addressed:

3.1.1. Patients with a rare disease and their family members are seeking information about their disease, possible treatment options, measures for social and economic assistance etc. Orphanet[55], the European portal website for rare diseases and orphan drugs should provide in theory the bulk of information on rare diseases from all over the EU. But up to now, it has no Dutch translated version (see measure 3.2.) and it is centrally managed and serviced from France. As such, very specific Belgian information (for example on reimbursement schemes, specificities about Belgian access to orphan drugs and treatment etc.) will not find its way in Orphanet. Moreover, the user friendliness of Orphanet for patients and the general public is questioned. On the other hand, it is certainly not a realistic option to replace Orphanet by a national Belgian website with similar content, as a lot of context will inevitably get lost.
Also other European websites with information on rare diseases (like the EU Public Health website or the EMA website) are in general not adapted to be used by patients or lay persons.

Description of the measure:

3.1.2. **The setup of a national portal website which provides various classes of users (patients, health care professionals, general public) with adapted information on rare diseases by providing links to validated existing information sources (including Orphanet)** was already suggested in the Recommendations and proposed measures for a Belgian Plan for Rare Diseases – Phase I.

This portal website should fulfil the following criteria:

- be available in at least 2 languages (FR, NL), possibly up to 4 languages (FR, NL, GE, ENG);
- have a clear, user friendly structure, tuned to specific audiences (patients, health care professionals, general public);
- have an easy to use content management system;
- link to validated sources of information (INAMI/RIZIV, FOD/SPF, patients' organisations, …);
- contain actual information on aspects of rare diseases not available in Ophanet;
- patients' organisations should be involved in the set up and the management of the website;
- could ultimately develop into an extranet type communication platform between Centres of Expertise, Centres for Rare Diseases, Centres for Human Genetics and the Platform for Rare Diseases.

3.1.3. The website should be hosted by an organisation which can adhere to the following conditions:

- be able to guarantee continuity of the service;
- be involved in rare diseases;
- be located in Belgium and be familiar with the Belgian administrative and policy situation on rare diseases and orphan drugs;

55 www.orpha.net

- be able to keep the information on the portal site actual in all of the languages (2 to 4);
- keep in contact with all relevant stakeholders (Patients' organisations, Centres of Expertise, Centres for Human Genetics, industry, administration, sickness funds…) in order to gather validated information;
- have the necessary qualified personnel, technical expertise and information sources;
- be independent, autonomous and objective;
- make a yearly report to the Platform for Rare Diseases on the progress and activities;
- if service is stopped, all information and knowledge should be transferred at no costs to the organisation which takes over these activities.

Expected impact:

3.1.4. Patients with a rare disease are guided towards validated and updated information.
Independent information instruments like websites are an important tool for patient empowerment.
First and second line care providers can find information on rare diseases and addresses for referral.
Centres of Expertise, Centres for Human Genetics, the proposed Platform for Rare Diseases, governmental organisations involved with rare diseases and other stakeholders get a centralised medium to disperse information to patients and other target audiences. Also the general public would have access to information on rare diseases.

Aspects related to timing and implementation:

3.1.5. As indicated earlier, the proposal for this measure was already included in the Recommendations and Proposed measures for a Belgian Plan for Rare Diseases - Phase I. Based on these proposals and a proposition by the Minister of Social Affairs and Public Health, a sum of 100.000 Euro was foreseen in the 2011 RIZIV/INAMI budget for a new initiative to create a portal website for rare diseases. The portal website will be created in collaboration and coordination with other initiatives aimed at improving the access and the quality of information, as they are foreseen in the Programme for Chronic Diseases.

Aspects related to costs:

3.1.6. A sum of 100.000 Euro was already allocated in the RIZIV/INAMI budget 2011 for this new initiative to create a portal website for rare diseases.
For the daily management of national portal website, content provision etc. a budget of 100.000 Euro/year should be foreseen in later years.

More background on the budgetary aspects are included in annex 8.

Measure 3.2. Support for Orphanet Belgium

Issue addressed:

3.2.1. While Orphanet's headquarters are located in France, Orphanet operates through a network of partner teams in the different countries that are responsible of collecting information on expert services and research on rare diseases.
Orphanet has earned worldwide recognition as a comprehensive reference information source on rare diseases. It has approximately 20.000 visitors every day, among them 300 Belgians. Though initially developed for health professionals (GP's, specialists,…), current Orphanet's visitors are 2/3 professionals and 1/3 patients. The website is considered by all stakeholders to be valuable and it has become the preferred partner of DG Sanco.

3.2.2. The Belgian Orphanet team is currently located at the Centre for Human Genetics of the UZ Leuven. Current progress of the Belgian database is limited due to insufficient funding (and thus manpower). The current limited European support should be complemented through national support. Switzerland, Italy, Spain and Germany already provide national support for the database.

Description of the measure:

3.2.3. It was already suggested in the Recommendations and Proposed measures for a Belgian Plan for Rare Diseases – Phase I that Orphanet (or parts of it) should be translated in Dutch (it should be investigated whether the Netherlands is interested in a joint translation of Orphanet). Currently, Orphanet is available in French, English, German, Italian and Spanish. After translation, Orphanet will become a valuable information source for all Belgian patients and their relatives, as well as for the general public.
It was furthermore proposed to support Orphanet Belgium with national funding to supplement the limited European support.

Expected impact:

3.2.4. Orphanet is the European source on all medical and other aspects of rare diseases. By implementing this measure it will become available to all Belgian citizens in the official languages of this country.
When fully developed, the Belgian information in the database can be an extremely valuable tool for Belgian health professionals and patients.

Aspects related to timing and implementation:

3.2.5. The Belgian authorities have decided to support the further development of Orphanet Belgium in the framework of a general proposal approved by DG Sanco. This support will be coordinated by the Belgian Federal Public Service (FOD/FPS) on Health, Food Chain Safety and Environment, in collaboration with the WIV/IPH.
Furthermore, it was decided by Ms. Laurette Onkelinx, Minister of Social Affaires and Public Health to start implementation of a new initiative in 2011 on the basis of the proposed measure and to allocate a budget from RIZIV/INAMI of 100.000 Euro in 2011.
Orphanet Belgium would be jointly managed by the Scientific Institute for Public Health and the Federal administration (FPS).

Aspects related to costs:

3.2.6. The costs included in the budget for this measure are an investment cost of 70.000 Euro for the translation of the patient-relevant data of the Orphanet website and an operating expenditure of 75.000 euro/

year, which would cover a salary cost and provide for a budget of 5.000 Euro/year for translation and other expenses.
This cost is normally part of a separate budget that was approved as part of the Belgian contribution to the EU-level project Orphanet and its financing. As it is relevant and part of this whole set of recommendations and proposed measures, it is included here.

More background on the budgetary aspects are included in annex 8.

Measure 3.3. Development of a communication plan on rare diseases

Issue addressed:
3.3.1. The two measures above are linked to specific communication instruments that need to be developed and are necessary investments to make large amounts of information available to various potential target groups. Communication is however a wider challenge that needs to be addressed as it is essential for the success of the Belgian Plan.

This challenge has various dimensions:
- The rarity of the diseases is setting the challenge at the level of communication. If it is unknown, you cannot diagnose nor treat the disease. Most of the challenges the health care system faces when dealing with rare diseases are linked to communication.
- Most of the measures proposed in this document, need to be known by those who are involved in implementation and those who could benefit from them. This is particularly the case with measures 1.1., 1.2. and 1.3. The foreseen networks of Centres of Expertise, Centres for Human Genetics and Liaison network for Rare Diseases have to be known to the medical care professionals in the first and second lines, and to the patients alike. Setting them up, without making sure everybody knows about their existence and how they can be of help, means poor utilisation of resources.

3.3. 2. The need for communication actions will change in nature during the course of the implementation of the Plan. This is why the measure proposed is to set up a communication plan that would be annual and flexible to adapt to needs.

Description of the measure:
3.3.3. **To develop an annual communication plan in support of the implementation of the future Belgian Plan along following principles**:

Overall objectives
- create a broad awareness for the concept of rare disease;
- ensure that anybody (patient, parent, medical professional,…) knows the way to the entry points and the network of CE, CHG and LRD, in case of difficult diagnosis;
- ensure that anybody (patient, parent, medical professional,…) can find appropriate information on their rare disease, particularly that they find the way to the portal and Orphanet;
- contribute to a change of attitude of both patients (more empowered) and medical professionals (more openness, more multidisciplinary, more cooperative).

Targets

Target groups for the communication are broad, and annual plans should probably concentrate on specific target groups to maximise efficiency.

Target groups at the national level include:

- the general public;
- patients suffering from a rare disease (and their families);
- patients' organisations:
  - ◇ pathology based associations;
  - ◇ patient platform organisation;
  - ◇ patient alliance organisations;
- medical professionals – both individuals and their associations:
  - ◇ first line medical care;
  - ◇ second line medical care;
  - ◇ hospitals;
  - ◇ university hospitals;
- academia
  - ◇ education (medical and paramedical);
  - ◇ permanent education (medical and paramedical);
- researchers;
- decision makers;
- opinion leaders.

At the European level:

- Centres of Expertise and Reference Centres;
- the research community;
- European institutions;
- EU level patients' organisations;
- EU level industry associations.

Main messages for each target group

Main messages to be communicated should be clearly defined in each annual plan, and adapted to each target group. They should focus on rarity, the need for a multidisciplinary approach and reduce the barriers to contact and cooperate with CEs, LRDs and CHGs.

Means

The means considered should be flexible in the understanding that the Portal and Orphanet are two essential means covered by the measures above.

The communication plan therefore would need to concentrate on two types of means primarily:

- relations with the press: to ensure the messages of the Belgian Plan for Rare Diseases are transmitted through various media;
- campaigns: whether annual or ad hoc. Such campaigns should as much as possible be executed in partnerships to maximise impact for the means invested. The rare disease day, and as a consequence strong cooperation with RaDiOrg.be, should be part of each annual communication plan;

- as part of the means, it is recommended to develop a 'brand name' to communicate the existence of the network of RD diagnostic and treatment centres at university hospitals. Such an approach is essential to attract the attention of both patients and medical professionals that they can easily remember where to go when they are 'lost'. These entry points into the care system should strongly be advertised.

Expected impact:

3.3.4. The impact expected is:

- a stronger awareness among the various target groups of:
  - ◇ the concept of rare diseases and the need for a specific approach to ensure patients with rare diseases are not discriminated;
  - ◇ the existence of a Belgian Plan for Rare Diseases;
  - ◇ the existence of the Portal Website and of Orphanet;
  - ◇ the existence of the networks of CEs, CHGs; and of the LRD;
- more openness among medical professionals, particularly towards a multidisciplinary approach (needed for the patient with a rare disease) and to cooperation (across disciplines, institutions and care levels);
- better empowered patients: aware of their rights, capable of finding the appropriate information and to take a bigger role in the decision-making process.

Aspects related to timing and implementation:

3.3.5. The implementation would be the responsibility of the management team under the suggested Platform for Rare Diseases. It is proposed that one person in that team would have formally the responsibility of the communication actions, supervising the establishment and implementation of the annual communication plan, as well as the activities in measures 3.1., 3.2., and 4.3.

Aspects related to costs:

3.3.6 The communication plan will be flexible, and lead to yearly objectives and focus. It is suggested by the Fund that the management of the communication plan will be the responsibility of the team supporting the suggested Platform for Rare Diseases (see measure 10 and the budget for management of the Plan).

Still, a separate budget is foreseen for the investment-related activities in communication. This includes: a budget for public relations towards the press, a budget for large campaigns (including support to Rare Disease Day), a small budget to cover miscellaneous communication actions.

The budget for measure 3.3. is estimated at 1,7 million Euro covering a period of 5 years. The highest budgets are foreseen in year 2 and 3 after the implementation of the future Belgian Plan for Rare diseases, specifically aimed at campaigns making the of the networks of CEs, CHGs and LRD known to the public.

Area 4. Patient empowerment

Patient testimonials

"When our daughter, who has cystic fibrosis, was a teenager, the paediatric pulmonary specialist encouraged her to take responsibility for her own treatment. I brought her to her appointments but stayed outside in the waiting room. At the beginning, I was not happy about it but I came to believe he was right."

"My first contact with the patients' association was when I got their regular bulletin. It didn't seem to me to be a good idea. It mentioned disabled children and I didn't see myself as the mother of a disabled child! It was only after I met someone from the association that I could understand their interest in it. Over the years, I have found it to be of great help and it even gave excellent legal support when I had to go to court to defend my daughter's rights after a decision by the consulting doctors."

"The Belgian Association to Fight Cystic Fibrosis has built up many years of positive experiences through organising discussions between leading centres. For a number of years now the Association has visited all these centres and looked at how they work on the ground. These visits create opportunities to share ideas, the Association can bring together their comments or draft responses on the basis of their experiences of how other centres work. These direct (and close) contacts between the Association and the Centre are more personal than peer review processes in large groups, and they can be used alongside the peer review process to bring more questions and/or uncertainties to light." **56**

"Because I suffer from myasthenia gravis I have to be extremely careful with anaesthetics and I certainly must not be given certain medications. In other words: if for any reason I do need to be anaesthetised or treated, it is vitally important that the doctors should know that I have this condition and take it into account when choosing medications. If they do not do so, I will be exposed to serious risks. In the hospital where I am treated it is written on my file in large letters. But what if I ended up in another hospital for some reason? And what if I were not able to explain at that time that I am a myasthenia patient? That is my greatest fear. I do keep a card that I have made myself together with my identity card, but still... How can I be certain that the emergency services or whatever will go looking for that?" **57**

56 *Knelpuntennota zeldzame aandoeningen, Vlaams Patiëntenplatform, 2009, p.41, www.vlaamspatientenplatform.be/www/component/option,com_docman/task,cat_view/gid,46/Itemid,98/*

57 *Idem*

Introduction

4.1. Empowerment is one of the areas addressed in the Council Recommendations of 8 June 2009.[58] Empowerment is the process of increasing the capacity of individuals or groups to make informed choices and to transform those choices into actions and outcomes. Actions in the field of rare diseases contributing to patients' empowerment should be a moral duty, based on solidarity and social justice, in each National Plan or National Strategy for Rare Diseases.
As a result of empowerment, patients with rare diseases have in many cases played an active and instrumental role in determining research projects and shaping health care policy. In addition, empowerment may result in better management of the daily needs of patients and better adherence with care protocols, in coping with the associated psychological conditions and in improving social inclusion. Promotion of education and of work participation is also an important action to foster the psychological development of rare disease patients and their families.

4.2. Patients' organisations are a crucial actor in the empowerment of patients with a rare disease. They play an important role in offering information and assistance to patients, and putting rare diseases on the research and health care policy agenda. Due to the large number of different rare diseases there are over 1.700 different rare disease patients' organisations in Europe and close to 150 in Belgium, alone. Many of these organisations are member of national alliances (in Belgium RaDiOrg.be) and/or of broader patient platform organisations (like the Vlaams Patiëntenplatform (VPP) or the Ligue des Usagers des Services de Santé (LUSS)). Most national alliances are affiliated to European umbrella organisations, the most important one being EURORDIS.

Supporting documents:
All proposed measures in this area originate from a workshop with patients and patients' organisations organised by the Fund for Rare Diseases and Orphan Drugs. This workshop took place in Brussels in December 2010. A report of the workshop 'Living with a rare disease – patient empowerment' (Nl/FR) can be consulted on the webpage of the Fund Rare Diseases and Orphan Drugs (supporting documents) via *www.kbs-frb.be*.
This supporting document was submitted by the working group on 'Information and patient empowerment'. Like all other supporting documents submitted by individual working groups, it has not been validated by the Management Committee of the Fund.

Measure 4.1. Empower patients in their relation to health care professionals

Issue addressed:
4.1.1. The relation between patient and care provider is seldom a relation in which both parties regard each other as equal interlocutors. However, patients should be offered the opportunity to enter into a partnership with their care provider based on the principles of 'shared care'. In this partnership the health professional is the expert on the disease and the patient the expert on his own life.
Patients should be made aware of the fact that they can make conscious choices themselves and that they should participate in the decisions on their disease path, in dialogue and partnership with their health care

58 *Communication from the Commission on Rare Diseases: Europe's Challenges, sec(2008)2713, http://ec.europa.eu/health/ph_threats/non_com/docs/rare_com_en.pdf and Council Recommendation on an action in the field of rare diseases, Official Journal of the European Union, 2009/C 151/02, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF*

providers. Conditions for such an empowerment are that patients have access to qualitative health care and are offered sufficient, correct and adapted information. The latter is a major prerequisite for informed consent decisions.

4.1.2. Evolving towards shared care depends largely on a relationship of trust between the patient and the care provider. Patients should be able and prepared to express their feelings, expectations, fears and hopes; the professional care providers should be empathetic with the patient, ready to (truly) listen, and be prepared to take decisions in consent. Both patient and provider should communicate transparently and in full openness.

4.1.3. An honest and open relationship is also an enhancing condition for therapy adherence. The care provider should communicate openly on the therapy options, providing sufficient and adapted information on the functioning, advantages, disadvantages and uncertainties of the therapy (also of the medication). The patient should be prepared to express what his ideas and feelings are on following the prescribed therapy strictly (or not). This is only possible in a relationship of trust in which care provider and patient discuss and decide together on the therapy.

4.1.4. Doctors, and other care providers, should communicate in an open, meaningful and transparent way with their patients, respect the autonomy of the patient and be prepared to come to shared decisions on the basis of equality and concordance. This is in essence not specific for care providers dealing with rare disease patients but applies to all health care professionals. As a result, this call for partnership between patient and professional caregiver is not withheld as a concrete proposal, but it is considered an obvious part of the normal relationship between the two parties. If necessary, care providers should be (re-)trained accordingly (see also area 5).

Description of the measure:

4.1.5. In order to empower patients in their relationship with professional caregivers, a number of submeasures (although not exhaustive) are proposed:

Measure 4.1.a. Patients who might feel uncertain, timid or sometimes confused during consultations, will be offered instruments and tools to help them in their communication with professionals. These instruments:

- can take the form of checklists, diaries, etc.;
- serve as guidance instruments during the consultation;
- will ensure that patients do not forget to express the questions and remarks they have during the stressful moments of the consultation;
- will be jointly developed by the Centres of Expertise and the relevant patients' organisations.

Measure 4.1.b. Patients should be offered the possibility to ask questions outside of the normal consultations:

- patients should have the feeling that they can go somewhere with their questions and rely on a solid answer;
- this support could take the form of a permanent helpline, which can be reached by telephone of e-mail. This helpline could be set up and supported by the network of Centres of Expertise and Centres for Human Genetics. These Centres have the necessary expertise and knowledge, and the whole network is sufficiently staffed to allow for the management of such a communication channel.

Measure 4.1.c. Give Centres of Expertise, care providers and patients' organisations the explicit task to inform patients in a meaningful way about their treatment, including medication, devices, diet, hygiene, etc. with the aim to enhance adherence:

- companion contact has shown to improve adherence to therapy. Experiences from fellow patients on medication, usefulness and/or side effects of certain treatments, aspects of quality of life, etc. are by many patients considered as valuable. It is therefore important that patients can meet each other and exchange those experiences. Therefore it is useful for Centres of Expertise to organise a patient information point in their consultation rooms, allow access to representatives from patients' organisations during consultation hours, and/or organise a yearly patient day in collaboration with the relevant patients' organisation(s) (see also measure 4.2.)
- also caregivers, especially in Centres of Expertise, play an important role in therapy adherence. Patients should understand their treatment and have the feeling that therapy adherence is a topic they can discuss with their professional caregiver. An open and trusty relationship is paramount to this. Also in the proposal for resolution submitted to the Belgian Chamber of Representatives on 21 December 2010, the quality of the relation between patient and professional caregiver is seen as an important factor to increase therapy adherence.[59]

As it can be expected that CEs, CHGs and LRD will develop a closer working relationship (see also measure 4.2.) it can be expected that this lists of topics will be further expanded and made more specific towards diseases/groups of diseases during the course of the Plan.

Expected impact:

4.1.6. Patients will feel reinforced in their relation with their care provider.
Patients who are insecure during consultations, will be more comfortable with the proper auxiliary tools and will address the questions they consider themselves as being important.
Patients have access to an information service where they can find valid answers to their questions.
Therapy adherence should be a topic which can be discussed between patient and care provider. Therapy adherence can be improved by adapted communication, a trusting relationship between patient and care provider, shared care decisions and regular companion contact.

Aspects related to timing and implementation:

4.1.7. The measures under recommendation 4.1. should be implemented gradually from the start-up of the first Centres of Expertise and could be supervised by the suggested Platform for Rare Diseases in close collaboration with the patients' organisations and the Centres.

Aspects related to costs:

4.1.8. Responsibilities and costs will be at the level of the network of CEs, CHGs and LRD on the one hand and patient organisations on the other hand. Costs linked to this measure can therefore be part of measure 8.1., and/or of measure 4.2.

59 *Resumed 'Voorstel tot Resolutie tot verbetering van de therapietrouw bij patiënten', Belgische Kamer van Volksvertegenwoordigers, doc 53 0907/001/'Proposition de Résolution relative à l'amélioration de l'observance thérapeutique des patients', Chambres des Peprésentants de Belgique, doc 53 0907/001' deposited by Ms. Maggie De Block in follow up of an earlier resolution deposited by Ms. Yolande Avontroodt.*

Measure 4.2. Enforceable patient participation at the start up, functioning and evaluation of Centres of Expertise

Issue addressed:

4.2.1. In many of the current Reference Centres ('CF', 'Metabolic', and 'Neuromuscular' who have a convention with RIZIV/INAMI), as well as in most Centres of Human Genetics, patients and their representing organisations are only seldom consulted. This is not logical, as the proper management and treatment of these patients forms the 'core business' of these Centres. Who else than the visiting patients (organisations) know the strong points and weaknesses of each Centre? Who else than patients (organisations) know what can be improved in the functioning of the Centres?

4.2.2. Patient participation and involvement in the current Centres is often minimised by denying access to patient representatives in Boards or Advisory Boards. In some Centres where patients have a seat in these commissions, but patients have the feeling that their remarks and comments are often ignored and disregarded. There are also Centres where new patients are not even informed about the existence and utility of patients' organisations.
In short, the relation between patients' organisations and the current Centres depends largely on the goodwill of the physicians and the (hospital) directors.

Description of the measure:

4.2.3.The right of patients and their organisations to participate – to have a voice – in the set-up, functioning and evaluation of Centres of Expertise should be enforceable at the following levels:

- advice from patient(organisations) should be sought during the setting up of new Centres of Expertise:
  - ◇ the specific needs of the patients with a specific rare disease or a specific group of rare diseases should be mapped and documented based on a consultation of patients and their relevant organisation (if it exists);
  - ◇ the type of staffing of the Centre of Expertise on that specific disease or group of diseases, and the organisation of the multidisciplinary patient management must meet those needs.
- a representative of the patients should be included formally in the Board or relevant Advice Boards in every Centre of Expertise. His/her contribution should be taken into account in the policy and functioning of the Centre;
- a procedure should be foreseen that patient representatives have the right to notify a monitoring official body (i.e. the suggested Platform for Rare Diseases (see measure 10.1.) or a RIZIV/INAMI commission) if the Centre of Expertise does not function according to the agreements stipulated in the convention and the criteria list for recognition;
- patients and patients' organisations should be involved during the periodic evaluation of the Centres of Expertise;
- each Centre of Expertise should organise in its consultation room a patient information point and/or create the possibility that a representative from a patients' organisation can be consulted by (new) patients.

Expected impact:

4.2.4. By involving patient representatives in the working of the Centres of Expertise, the quality of patient centred care will improve since enforceable patient participation in the Centres of Expertise ensures a focus on real patient needs.

Aspects related to timing and implementation:

4.2.5. Patient participation should be included from the beginning of the implementation of the various proposed measures of the future Belgian Plan for Rare Diseases.

Aspects related to costs:

4.2.6. To cover the costs of this measure we propose to earmark a fund that would be used to cover the value delivered by patients and patient organisations involved in this process. To avoid potential conflicts of interest, this could be a fund that is managed centrally (by the Platform for Rare Diseases).
The initial budget proposed is 120.000 Euro/year (see Tables 1 and 2 in Chapter 5). This budget is however increasing over time (to 200.000 Euro in the fifth year) as the expectation is that the value of the patient contribution to the care of patients will be appreciated and that more will be asked to patients and their patient organisations over time[60]. This is also the case if the working group proposed in measure 4.3. leads to more initiatives.

More information on budgetary aspects is included in annex 8.

Measure 4.3. Improvement of the collaboration between patients' organisations

Issue addressed:

4.3.1. The cooperation between patients' organisations is not always proceeding optimally. Especially in the domain of rare diseases, it is of momentous importance that forces between patients' organisations are joined at all levels.
Why is efficient collaboration so difficult? One factor is that patients' organisations for rare diseases are usually small because for most disease there are only few patients. Therefore these organisations are most of the time managed and supported by volunteers (very often informal carers, family members, or even patients themselves). Very often, patients' organisations do not know from each other's' existence and are not aware of possible common interests. Also the added value of umbrella organisations, patient platforms or organisational supporting agencies is not always recognised. All this hampers a good, smooth and efficient cooperation, impedes the evolution towards further professionalization, and leads to further fragmentation which in turn paves the way to ignorance and even internal competition. This has without doubt a negative impact on the role these organisations can play in the construction of proper health care provisions for patients with a rare disease.

Description of the measure:

4.3.2. It is proposed that the Platform for Rare Diseases sets up and supervises a working group which provides a forum for:

- developing a charter with a code of conduct and a minimal set of quality assurances (the presence of statutes, elections of governing structures, etc.) for patients' organisations involved in rare diseases. Individual organisations who sign this charter and who function according to the provisions of the charter, can propagate this as a sort of 'quality label';

60 *This could also lead to a transfer of funds from CEs to POs, therefore with a zero effect on the budget.*

- making practical arrangements between patients' organisations, umbrella organisations and patient platforms on cooperation, task allocation, mutual support, common policy development etc;
- a brain storm on how patients' organisations could be formally recognised;
- developing a comprehensive plan on the role of patients' organisations in the care system for patients with a rare disease and discuss with the authorities the level of support needed to fulfil this role;
- exchanging experiences and good practices;
- and many other pending issues…

Expected impact:

4.3.3. The needs of the patients with a rare disease will be better defended.
The constructive role patients' organisations can play in the organisation of the care for patients with a rare disease will be made explicit and clarified.

Aspects related to timing and implementation:

4.3.4. It is expected that within three months after the establishment of the Platform for Rare Diseases, a workgroup dealing with the collaboration between patients' organisations should be set up. Within 6 months after the first meeting the charter should be finalised and within 18 months the comprehensive plan on the role of patients' organisations should be completed.

Aspects related to costs:

4.3.5. The costs of this measure are part of the management cost as it would be one of the working groups managed under the proposed Platform for Rare Diseases.

More information on the budgetary aspects is included in annex 8.

Measure 4.4. Ensure the development of an instrument for rapid communication of medical need in case of emergency

Issue addressed:

4.4.1. Patients with a rare disease can end up in a(n) (acute) situation in which it is important that they can (quickly) make clear that they have a specific disease and special needs. Obviously, during the admission to a hospital (possibly even abroad) or during a medical urgency, the emergency medical physician should be immediately aware of the specific situation of these patients.
But also at other places and occasions patients can have specific needs which they want to communicate in a more formal way.

4.4.2. Already for many years, patients and their representing organisations, and in particular patients with a rare disease, are demanding an instrument that gives them the possibility to communicate that they have a specific (rare) disease, that they have certain needs, or that certain treatments might be (life) threatening for them. The instrument is often referred to as a medical passport.
Although many patients' organisations, especially the ones dealing with rare diseases, have tried to bring this problem to the attention of policy makers, it is often considered not to be a health priority by policymakers, while it is for many patients at the top of their priority list. They are convinced that such an instrument could save (their) lives.

Description of the measure:

4.4.3. **In collaboration with patient organisations, the proposed Platform for Rare Diseases should put the development of a rapid communication instrument in case of emergency on the agenda of policy-makers, both at European level and at national level. In case a rapid development of such an instrument is not feasible at European level, an intermediary instrument should be developed at national level**.

This instrument should:

- contain or give rapid access to important data such as identity and address, diagnosis and data about the disease, blood group, indispensible medication and treatment, contra-indications, person to contact, treating physicians, Centre of Expertise…;
- preferably be developed at national and/or EU level and be in digital format. Caregivers in Europe should be aware of the existence of these instruments. If a person in an emergency situation is admitted to a hospital, they should look for such a, instrument. Ideally, such an instrument giving access to vital and lifesaving information is embedded in the European eID card.

Expected impact:

4.4.4. Such an instrument gives patients the opportunity to communicate their specific needs quickly, efficiently and in a formal way.
In case of medical urgencies, instruments like passports giving access to health information and/or urgency cards can save lives, especially in the case of rare diseases.
Such an instrument can be used as a legitimate ID for obtaining certain facilities.

Aspects related to timing and implementation:

4.4.5. Examples of medical passports or urgency cards in Belgium are the haemophilia card, the 'Pink card' of the Flemish League against Epilepsia or the pacemaker registration card. Examples abroad are the 'Carte de soin' in France and the European Medical Passport (EMP) which is written in 11 European languages.[61]
This measure has been investigated in the past for other diseases as well and at different institutional levels. Flanders even has an official decree on the 'eenvormige medische urgentiekaart' (uniform medical urgency card).[62] In practice this card is underused and no longer adapted to current needs.[63]

4.4.6. It is therefore advised that this measure would be investigated by the suggested Platform for Rare Diseases in the wider perspective of e-Health and/or eID at European level, in collaboration with national and international patients' organisations.
However, if it becomes clear that this dossier is not making sufficient progress at EU level (i.e. within a timeframe of 24 months after the implementation of the Plan), the Platform for Rare Diseases should start a national initiative, especially aimed at the development of an individual communication instrument for patients with a rare disease. At that time, an appropriate budget should be negotiated with the national authorities.

61 *Knelpuntennota zeldzame aandoeningen, Vlaams Patiëntenplatform, 2009, p.41, www.vlaamspatientenplatform.be/www/component/option,com_docman/task,cat_view/gid,46/Itemid,98/*

62 *Besluit van de Vlaamse Executieve tot vaststelling van de praktische modaliteiten ter uitvoering van artikel 4 van het decreet van 23 december 1986 houdende het invoeren van een eenvormige medische urgentiekaart, 1987062532/N, http://www.ejustice.just.fgov.be/cgi_loi/loi_l1.pl?language=nl&caller=list&la=n&fromtab=wet&tri=dd+as+rank&sql=dd+=+date'1987-06-25'*

63 *Answer of Mss. Inge Vervotte, Flemish Minister of Welfare, Public Health and Family to question 83 of Ms. Annick De Ridder on the uniform medical urgency card, Bulletin van vragen en antwoorden, Vlaams Parlement, 18, p. 1628-1630, http://docs.vlaamsparlement.be/docs/bva/2004-2005/va18-24062005.pdf*

Aspects related to costs:

4.4.6. The initial cost for the policy work at EU level falls under the budget of the Platform for Rare Diseases. The investment cost linked to a national set up in case the European eID-approach is not leading to results, is estimated at 50.000 Euro and included as an investment in year 3 (see annex 8). It could take the form a service contract (typically for service design), coupled with a working group who would define the terms of reference and monitor the service contract implementation. If sufficient progress is made at EU level, this budget post can be omitted.

More information on the budgetary aspects is included in annex 8.

Area 5. Training and education of health professionals

Patient testimonials

"Even now at the age of 54, I still meet a lot of doctors who have never seen the symptoms of this illness and who know absolutely nothing about it. Some of them ask if I have suffered burns. I explain to them that it is a genetic disease (dystrophic epidermolysis bullosa)."

"A doctor said that our daughter would not see her 15th birthday. She is now 27 and living her life independently."

"The dermatologists who first treated me told my mother that I would not live beyond my 5th or 6th year. When I reached that age, they postponed this limit to 12 years, then 18 years. When I was 30, I was again told that I wouldn't live until I was 50. Now I'm 53 and doctors have stopped saying these things!"

"I was 46 years old when I learned that my father's symptoms were caused by Huntington's Disease. At the time, in the 1990s, this disease was still not very well known especially in the French-speaking world. The diagnosis really bowled me over as I was informed of it without any warning; a doctor coldly told me over the telephone. I have since discovered that I could be affected too and so could my sons and the rest of my family on my father's side."

Introduction

5.1. The adoption of appropriate initiatives for training and education of health professionals is an important instrument to improve diagnosis and quality of care for patients with a rare disease. The need for training does not refer only to clinical capacity, but also to the ability to communicate with patients (see also area 4), and to clinical and organisational aspects (e.g. diagnostic strategies, referral of patients, etc.). The latter may cause dangerous delays in the provision of adequate care.

5.2. Training and education of professionals can be aimed at different target groups, according to the role they play in rare disease care. All health care professionals should be made aware of the existence of rare diseases, the difficulty of diagnosis, the specific organisation of the health services to assure appropriate care and of the specific needs of rare disease patients.

Measure 5.1. Integration of education and training on rare diseases (and orphan drugs) in the Faculties of Medicine and Pharmaceutical Sciences, in Paramedical Institutions and in the continuous medical education of health care professionals.

Issue addressed:

5.1.1. Education and teaching on rare diseases are critical factors in optimizing care for patients with these conditions. Education on rare diseases is relevant, not only for medical students, but should also target the wide spectrum of other health care professionals (speech therapists, nurses, physiotherapists, psychologists, pharmacists,…). The aim of this measure is to inform all students involved in disciplines related to health care on rare diseases, on the available rare disease resources – such as Orphanet, the portal site, the role of patients' organisations – and on the existence of orphan drugs.
Education on rare diseases should also form an integral part of the continuous medical education of health care professionals. Special attention should go to medical professionals involved in the services of 'Child and Family' (Kind en Gezin/ l'Office de la Naissance et de l'Enfance) and the socio-medical supervision at school (CLB/les Centres PMS).

5.1.2. The targets for education and teaching include providing health care workers with appropriate skills for managing rare diseases, such as shared decision making, an unprejudiced attitude towards unexplained symptoms and a preparedness to refer patients.
The main objectives of teaching and education of all the health care professionals comprise: to distribute knowledge on rare diseases and orphan drugs (definition, characteristics, properties), to increase awareness about them, to illustrate the relevance of rare diseases, to inform and educate on orphan drugs and to motivate to diagnose and treat rare diseases.

5.1.3. In addition, specific attention should focus on the Belgian health care structures about rare disease and the international (European) dimension. Also, the visibility of the Centres of Expertise, the Centres for Human Genetics and Centres for Rare Diseases should be increased. Finally, education should facilitate access to resources for rare diseases.

5.1.4. In view of their first-hand expertise, patients and patient organizations should be actively involved in education on rare diseases. Already, these organisations play an important role in the guidance and accompaniment of master and doctoral students during their research and the writing of their theses.

Description of the measure:

5.1.5. **Education and teaching on rare diseases should be integrated in the curricula of health care professionals and in the continuous medical education of health care professionals** (i.e. medical doctors, paramedical professionals, nurses, pharmacists,…).
Rare Diseases comprise thousands of conditions. As a consequence, providing training on all rare diseases is an unrealistic objective. Educational institutes should rather focus on generic elements which are common to groups of rare diseases.
The practical implementation of these recommendations is at the own discretion of the educational institutions and professional organizations:

- Nevertheless, Faculties of Medicine should target on illustration of the relevance of rare diseases through clinical case studies. Faculties should integrate education on rare diseases in Master and postgraduate

training ('Manama'/'Master Complémentaire'). Training in the application of Orphanet is essential in this perspective.
- Faculties of Pharmaceutical Science should develop training on orphan drugs (including the possibilities of home care for some orphan drugs) and training in the application of Orphanet.
- Paramedical institutions should integrate education on rare diseases in the curriculum with specific attention to patient empowerment. Training in the application of Orphanet could be added.
- The suggested Platform for Rare Disease should evaluate the need for standardization in training and education. Considering the current situation, they should distribute recommendations on rare disease education and teaching. They should survey the existing teaching and education on rare diseases and evaluate (and reorient if needed) education initiatives on rare diseases.

In the long run, a homogeneous educational program throughout the country or similar level of education on rare diseases might be considered.

5.1.6. To enhance the knowledge and to encourage the continuous formation, Centres of Expertise, Centres for Human Genetics and Centres for Rare Diseases should establish guidelines for specific rare diseases and group them in an interactively consultable on-line database. They should be in charge of the dissemination of new clinical, fundamental or translational developments in the field of rare diseases, the introduction of novel orphan drugs, the initiation of clinical trials or research projects, the availability of novel diagnostic tests,….
A working group has been recently created by the BeSHG (Belgian Society for Human Genetics): clinical geneticists and genetic centres representatives will also elaborate national guidelines for specific rare diseases.

5.1.7. Professional organizations should prioritize rare diseases in their activities (annual meetings, publications, research and clinical projects…). They should develop interaction with rare disease Patients Organizations and train their members in the application of Orphanet.

5.1.8. Collaboration between patient and professional organizations needs to be actively pursued in order to optimize the visibility of rare diseases: interactive workshops during annual meeting could be a good opportunity to follow and to develop these links.

Expected impact:

5.1.9. Education and teaching on rare diseases will improve the diagnosis and treatment of these conditions and contribute to patient empowerment. The use of Orphanet and networking will be more easily integrated into daily clinical practice.

Aspect related to timing and implementation:

5.1.10. The integration of rare diseases in teaching and education could start quickly, preferably the year after the launch of the Belgian Plan for Rare Diseases. Several Deans showed their interest and confirmed the need of teaching on rare diseases.

Aspect related to costs:

5.1.11. A budget of 50.000 Euro/year is foreseen for this proposal. This budget is especially intended for the creation of education and training material, and to reimburse patients' organisations who participate to these initiatives. Normally this budget should be provided by the Communities and could be managed by the proposed Platform for Rare Diseases.

More information on budgetary aspects is included in annex 8.

Measure 5.2. The introduction of rare diseases in the continuous medical education (CME) of care providers and approved in the current accreditation system by RIZIV/INAMI.

Issue addressed:

5.2.1.The message that continuous education on rare diseases for health care professionals is necessary, should be reinforced and officialised in some way.

Description of the measure:

5.2.2. **The organisation of courses on rare diseases specifically aimed at general practitioners and recognised by the current accreditation system (under the topics ethics or economy) should emphasize the necessity of continuous education and training on rare diseases for physicians**.

This should also concern professionals who participate in Patients Organizations and who are involved in these associations. They could benefit from the accreditation, in regards to the scientific information and formation that they share.

5.2.3. The networks of CEs, CHGs and LRD should be stimulated to organise these courses.

Expected impact:

5.2.4. Even if GP's, specialists or other care providers are not often confronted with rare diseases, a better knowledge will help them to think about rare disease and to take in consideration some unusual symptoms of their patients. At term, it could avoid medical roaming and reduce costs.

An official recognition of the implication of a practitioner in a Patients Organization dedicated to rare diseases would be a positive signal and would participate to the development of empowerment.

Aspect related to timing and implementation:

5.2.5. After approval by RIZIV/INAMI, this measure could be implemented immediately.

Aspect related to costs:

5.2.6. A budget of 30.000 Euro/year is foreseen. This budget will be managed by the proposed Platform for Rare Diseases and will be allocated to third parties (networks of Centres, or others) organising these courses.

More information on budgetary aspects are included in annex 8.

Area 6. Improving access to and financing of diagnosis

Patient testimony

"I am over 50 now. The diagnosis of the genetic form of my illness (dystrophic epidermolysis bullosa) was made only 10 or 15 years ago. Skin and blood samples were taken in a Brussels hospital and sent for analysis to Fribourg. Since then, we have known the exact cause of the illness. The tests lasted two years."

Introduction

6.1. When looking at the use of technologies for testing, the rarity of the disease has two main consequences:
in a number of cases the test can only be done or is best done abroad, for example because the proper expertise is not available in Belgium. This goes against 'normal' practice. In the case of rare diseases this can lead to adverse effects as patients face barriers (juridical, financial, practical) to get the tests done;
some technologies are disappearing in Belgium as hospitals and labs consider that these tests are 'not economical' (cost versus reimbursement).

6.2. Two sets of measures are therefore proposed:
one to cover DNA testing. This is essentially testing managed by genetic centres meant for diagnosis, but more and more often also for controlling the adequacy of a treatment.
the second set is to cover non-DNA laboratory testing as well as the use of other technologies in diagnosis and control of efficacy of treatment.

Measure 6.1. Adjustment of the system to allow DNA-samples to be tested abroad

Issue addressed:
6.1.1. The time that samples were handled as 'research samples' and tests performed for free by 'friends-scientists-informal-networks' is behind us. DNA testing has become a service that needs to be performed in a laboratory that has the expertise, that ideally is accredited, and that provides a service according to normal standards (within agreed turnaround time, with a full outcomes report, and the necessary quality standards).

6.1.2.Testing abroad is a necessary service as tests exist for thousands of rare diseases. Only a fraction of these tests are performed in Belgium. Specialisation of labs for DNA tests is recommended for Belgium, but will happen as well at EU level and even internationally. Such specialisation may increase the need of having to send samples abroad for testing. Volumes of DNA tests sent abroad will therefore probably increase.

6.1.3. Until now, the Belgian health insurance system did not allow the reimbursement as charging the system for tests performed on samples sent abroad is not legally foreseen. Reimbursement of such tests is only possible if the patients travels abroad (E112) and the test is reimbursed in that country. Sending patients is however not necessarily the best solution, neither for the patients (travel cost and time) nor for the health insurance system (significantly higher cost).

6.1.4. Based on information from the Centres for Human Genetics, some 846 tests were performed abroad in 2007 at a cost of 430.000 euro.

Description of the measure:

6.1.5. In the Recommendations and Proposed measures for the Belgian Plan for Rare Diseases – Phase I, it was therefore recommended that **for diagnostic testing[64] of DNA samples of patients and their relatives and for which in Belgium no specialized laboratory is available that can perform such testing, a special financial budget is granted to the Centres for Human Genetics (or other relevant Centres), to allow coverage of the costs of such testing done in a laboratory outside Belgium (if such laboratory can be found).**

The same should be true for the confirmation of screening results for relatives.

Expected impact:

6.1.6. The impact for the patient and his/her relatives is access to the right test, reimbursed as if the test was performed in Belgium (the cost of the test was sometimes charged to the patient).

Aspect related to timing and implementation:

6.1.7. This proposal was part of the recommendations and measures proposed during Phase I of the work of the Fund. Based on this proposal and a proposition by the Minister of Social Affairs and Public Health a sum of 550.000 Euro was foreseen in the 2011 RIZIV/INAMI budget. This new initiative will be integrated in a convention (contract) between RIZIV/INAMI and the Centres for Human Genetics in the context of the revalorisation of the genetic consult (a measure foreseen in the Cancer Plan).

6.1.8. It is expected that in the near future criteria and procedures will be worked out to ensure that the tests executed abroad are performed according to quality standards.

Aspect related to costs:

6.1.9 Following a consultation within the Medicomut regarding the nomenclature of genetic testing, a budget of 550.000 Euros was retained. It is proposed to foresee an increasing budget over time, as we expect an increase in volume, which will be partly compensated by a gradually reduced cost per test (due to lowering prices and better purchasing).

More information on the budgetary aspects are included in annex 8.

64 *Although only diagnostic testing is mentioned, this covers also tests performed before deciding on medication, or to control the effectiveness of a treatment (pharmacogenetics).*

Measure 6.2. Access and reimbursement of non-DNA testing and development of such technologies in Belgium

Issue addressed:

6.2.1. Diagnosis is a very important part of prevention, treatment or any follow-up step, especially in rare diseases where the confirmation of a diagnosis can sometimes take up to 30 years, and/or where proper monitoring may be crucial.

Diagnosis or its follow-up can be made on the basis of laboratory testing, but also by other *in vivo* or *in vitro* tests. Even physical parameters or their standardized measurement or the like can be important for confirmation of a diagnosis or for monitoring. Therefore, non-DNA diagnostic tests are defined to include all of the above acts.

6.2.2. Such diagnostic tests should be available and reimbursed in Belgium insofar possible. Patient payment contribution needs to be discussed. This area should also be integrated in the work done for chronic diseases in general.

Different types of problems have been defined linked to the rarity of tests to be performed for patients with rare diseases:

- some of these tests are not reimbursed as they do not appear on any nomenclature, or are not part of lump sum agreements between reimbursement authorities and labs;
- some technologies are disappearing, mainly because of the imbalance between cost and reimbursement;
- as for DNA tests, each lab confronted with the need to have a test performed abroad will take its decision based on its own policy: whether to have the test performed or not, and to charge the patient or not.

All these issues have been analysed in the context of the preparation of these proposed measures for the Belgian Plan for Rare Diseases, and experts and stakeholders have drawn lists of tests, identifying where competence is (still) available in Belgium, and eventual reimbursement issues. The proposed measures below are based on this first inventory.

Description of the measure:

6.2.3. **A list of important diagnostic tests should be drawn up and regularly updated. Apart from laboratory-based tests the list should also include other diagnostic tests, be it in vitro or in vivo,. This list can be drawn up by a group of experts and approved by RIZIV/INAMI. A mailbox for recommendations, issues and suggestions could be set up by the suggested Platform for Rare Diseases**.

6.2.4. **As a general rule, the diagnostic tests on the list should be reimbursed, without creating a preferential situation for rare diseases, however. For those tests for which this is not possible, a system of a defined annual budget should be set up**. Such defined annual budget should cover, under the supervision of a Belgian expert laboratory, payment and quality control of tests which are not reimbursed in Belgium, or which need to be sent abroad since expertise for this test is not available in the country.

6.2.5. A purchasing policy should be set up for more frequent tests where possible by the appropriate authority and should stipulate that, when a diagnostic test can be performed in Belgium, it should preferentially be done in (one) specific lab(s). For tests performed out of the country, it is recommended that a European purchasing policy is set up that all CEs and labs would need to apply: this policy should identify and negotiate with preferred suppliers who should be certified labs to guarantee quality. Belgium should ensure to have such EU reference laboratories recognized for its areas of strength.

6.2.6. It is important that the notion of diagnostic testing is also broadened to the area of research, development and access to biomarkers and diagnostic tests for use in conjunction with therapies.

Expected impact:

6.2.7. The impact for the patient and his/her relatives is access to the right test, properly reimbursed according to the same standards as tests for non-rare diseases and in accordance with measures taken for all people with a chronic disease.

Aspect related to costs:

6.2.8. Not enough information could be collected during the preparation of this measure to make an estimate of the budget impact. This measure potentially covers on the one hand a large number of technologies and tests, but on the other hand, a small number of patients. The budget included in the plan is therefore set at 1/3rd of the cost earmarked for the DNA tests sent abroad, or 330.000 Euro in the fifth year.

More information on the budgetary aspects is included in annex 8.

Area 7. Improving access to and financing of medical treatment

Patient testimonials

"At five years of age, M. participated in a clinical study," her mother said. "The results were obvious: suddenly with the treatment, her condition stopped getting worse. But the pharmaceutical company was bought out and the clinical trial was stopped along with study of the molecule which was deemed not profitable. Despite intervention from the Minister for Health, my daughter's treatment which had been working well was stopped." (M. has metachromatic leukodystrophy).

"Due to a lack of a treatment when I was small and even later, they used different improvised ointments and dressings. I came down with a lot of infections that set in in the wounds. Luckily, my mother was a doctor and her care meant I could avoid infections and their consequences which would have been fatal for me. It was only in the years after 2000 that the situation improved with the arrival of costly but efficient compresses. Now, after a long process, the special solidarity fund intervened and pays for this treatment."

Introduction

7.1. For a lot of patients with a rare disease, there is no treatment available in comparison to patients with a more common disease. The best example is the complex pathway for orphan drugs: in the 10 years since the legislation on orphan medicinal products exists, less than 70 have reached the market, which means that for only 1/100 rare diseases a specifically targeted drug is available.
Still, there are more than 700 research projects that received the orphan designation, and that are therefore in the process of being researched.
It should also be noted that patients are also being treated using other techniques, whether paramedical treatment, surgery, or the use of 'non-orphan' medicinal products. These products are very often used 'off-label', as they were not approved for the rare condition the patient is suffering from. This leads to special and unique situations that patients with rare diseases are facing compared to patients with more common diseases.
The priorities concerning new research and the development of new treatments, should be determined on the basis of the opinion of experts (bundled in the networks of Centres of Expertise). These should be based on the needs indicated by the patients and included in the lists drawn up by the CEs.

7.2. In this area different measures are proposed to reduce the discrimination of patients with rare diseases mainly by improving or speeding up access to treatment, when the treatment exists.
Different concepts are being used in this section which the reader needs to know. These concepts are:

- Clinical trial
- Compassionate use programmes
- Medical Need programmes
- Orphan drugs
  - ◇ designation
  - ◇ marketing authorisation
  - ◇ reimbursement
  - ◇ Off-label use of medicinal products

A definition of the concepts are given in annex 4.

7.3. The first series of six proposed measures cover the first three concepts: Clinical trials, Compassionate use and Medical need programmes.

Measure 7.1 is the most important one in this series of proposals.
The ultimate goal pursued by this set of measures is:

- to ensure that Belgium contributes to the effort of developing new treatments; clinical trials are an essential step in the process from research to treatment;
- to improve the situation of individual patients, who could potentially gain, through the clinical trials, compassionate use and medical need programmes an early access to a potential treatment. For rare diseases this is a critical element as there is very often no alternative treatment available;
- to increase transparency and circulation of information on the efficiency of novel treatments including by participation in the CAVOD program[65] at EU level;
- to protect patients which can be critical in 'grey zones' of medication use, where control agencies are not always aware of what is happening.

Supporting documents

Most proposals for measures in this area have been suggested by the working group responsible for working package 5 'Access to diagnosis, drugs, and treatment, and financing'. This working group has drawn up a document entitled 'Fifth draft work document following discussions in meetings of working party 5 on early temporary access and early temporary reimbursement'. This document can be can be consulted on the webpage of the Fund Rare Diseases and Orphan Drugs (supporting documents) via www.kbs-frb.be.
This supporting document, like all other supporting documents submitted by individual working groups, has not been validated by the Management Committee of the Fund.

65 *Improving access to orphan medicines for all affected EU citizens, Final Conclusions and Recommendations of the Pharmaceutical Forum, page 4, bullet 'Exchange of knowledge amongst Member States and European authorities on the scientific assessment of the clinical added value of orphan medicines.', http://ec.europa.eu/pharmaforum/docs/pricing_orphans_en.pdf*
and EAHC-tender 'The creation of a mechanism for the exchange of knowledge between Member States and European authorities on the scientific assessment of the clinical added value for orphan medicines', http://ec.europa.eu/eahc/health/tenders_H05_2010.html

Measure 7.1. Launch an information service on clinical trials, compassionate use and medical need programmes

Issue addressed:

7.1.1. Patients and the first line of medical care cannot access objective validated information about the possibilities for participation in clinical trials. At the moment, there is no such information available in a form that is adapted to either of these two target groups.

A database exists at the EU level with all clinical trials performed in EU. The Belgian part of this data-base is the responsibility of the FAMHP. The EU data-base has recently become available[66], but is not adapted to this target group.

Description of the measure:

7.1.2. **Set up an information service that would be neutral and objective, and provide information on**:

- **on-going (and finalised) clinical trials (at EU level);**
- **medical need programmes (at Belgian level);**
- **compassionate use programmes (at Belgian level).**

This information would be made available in an adapted form to:

- **patients;**
- **medical professionals.**

Setting up this information service should logically be the responsibility of the FAMHP.

Promoting its use and creating access could also be envisaged through the proposed portal website on rare diseases and Orphanet (Belgium).

Expected impact:

7.1.3. Main impact:

More patients participating in clinical trials, which leads to faster access to a potential treatment.

7.1.4. Additional impacts:

Better informed decisions from patients when they decide to participate in clinical trials.

- better information service by first line medical care professionals;
- more transparency for patients: even if a centre of expertise, or second/third line medical care professional would not inform the patient, both the patient and their first line GP can have access to the information.

Aspects related to timing and implementation:

7.1.5. Setting up such a service means a significant investment which will take time to be set-up. Target could be to have a pilot version of the information service available after 18 months, e.g. covering only the clinical trials in Belgium, and a full information service for both target groups at the end of year 3. For making this second level fully operational, there will be a need to change the legislation as to ensure that data collected can be used and information concerning approved and on-going medical need and compassionate use programmes are made available.

7.1.6. This information would need to be linked with the national rare disease registry. The standard set of

66 *EU Clinical Trial Register, European Medicines Agency, https://www.clinicaltrialsregister.eu/*

data for all rare diseases should include information and links to clinical trials, compassionate use and medical need programmes.

Aspects related to costs:
7.1.7 This measure is not expected to have direct impacts, neither negative nor positive, on the health insurance budget.
The implementation of this measure should normally fall under the remit of the FAHMP.
The investment related to the measure is however significant, and will probably lead to switches in the way resources are used within the FAHMP.

More information on budgetary aspects is included in annex 8.

Measure 7.2. Adapt existing legislation to increase transparency and availability of information from compassionate use and medical need programmes

Issue addressed:
7.2.1. An adaptation of the existing legislation is needed to allow the public availability of information concerning approved and ongoing compassionate use and medical need programmes as foreseen in measure 7.1. The adaptation of the legislation could also lead to a necessary improvement:
- to include the systematic follow-up of the patients included in these programmes;
- to register the follow-up data so that both positive as well as negative outcomes are available, the best use is made of scarce data, and the increase in knowledge on efficiency of treatment is transparent.

In order to avoid that companies would be discouraged to set up such programmes, it should be clearly defined who owns or who has access to the follow-up data on outcomes. As is the case for clinical trials, it is logical that these data are owned by the sponsor of the program. But at the same time, it is logical too that the data should only be used under the supervision of the Drug Agency.

Description of the measure:
7.2.2. **Adapt existing legislation to increase transparency and availability of information from compassionate use and medical need programmes**.

Expected impact:
7.2.3. Main impact:
More transparency for all stakeholders (patients, clinicians, authorities, companies,…) on the efficiency and the scientific value (including secondary effects and toxicity) of treatments.
A better access of patients to these programmes.

Aspects related to timing and implementation:
7.2.4. This could be done fast and is proposed to be realised within 12 months.

Aspects related to costs:

7.2.5 There are no costs and no health care budget impacts for this proposed measure.

Measure 7.3. Awaiting an adaptation of the EU clinical trials Directive, Belgium should pro-actively apply the so-called 'Voluntary Harmonised Procedure' whenever a request to launch a clinical trial in Belgium for an orphan drug is submitted.

Issue addressed:

7.3.1. The decision to grant an orphan designation to a drug is a decision taken at the EU level.
When the sponsor obtains this designation and invests further in clinical trials to prepare the market entry, they need to address all 27 Member States individually as this is a national responsibility. In the case of rare diseases, the need to spread the clinical trials over more countries is a must as the number of patients is low. This creates an additional barrier for the industry, and puts potentially Belgian patients at a disadvantage, as Belgium, because of its size might be less attractive to organise clinical trials for the sponsor.

7.3.2. This issue is being addressed at an EU level, but it will take years before an EU level solution is defined and operational (cfr. revision of the Clinical Trial Directive foreseen for 2013 -2014 best case scenario).
In the meantime, a procedure called 'Voluntary Harmonised Procedure' (VHP) has been set-up. This means that a single demand can be addressed to more than one Member State simultaneously. This is triggered at the initiative of the sponsor and is an informal cooperation between Member States.

Description of the measure:

7.3.3. The measure proposed is not to wait until an EU level consensus exists and to stimulate the use of the VHP at the Belgian level.
This means that **when Belgium receives a demand for clinical trials in Belgium for a drug with orphan designation or a clinical trial for rare diseases, it would systematically activates the scientific discussion as in the VHP with the other Member States concerned** (not necessarily the VHP procedure as such in order to take the advantages of the short delays in Belgium into account).

Expected impact:

7.3.4. Better design and higher efficiency in conducting clinical trials. This should speed up and facilitate the decision-making and therefore the access to treatment for patients.
It is also expected that more (Belgian) patients will have access to these clinical trials.
Aspects related to timing and implementation:
7.3.4. This measure could be implemented from the start of the Plan.

Aspects related to costs:

7.3.5 There is no budget impact on the health insurance system.

Measure 7.4. Improvement of the procedure how ethics committees come to a single opinion in the case of rare diseases

Issue addressed:

7.4.1. In the case of rare diseases, the need to spread the clinical trials over more medical centres in several countries is a must, as the number of patients is low. This means that several ethics committees need to give their advice. This can lead to serious delays in the development of a new drug.

Description of the measure:

7.4.2. **Attempts should be made to arrive at a better founded single opinion, by stimulating the interaction between the ethics committees in Belgium. A possible solution could be the establishment of a platform structure where ethics committees discuss delicate protocols.**
In the longer term, and in the context of the revision of the EU Clinical Trials Directive, one should try to have a similar system applied at EU level.

Expected impact:

7.4.3. Better quality of the decision making process for clinical trials and better protection of patients if and when clinical trials are stopped.

Aspects related to timing and implementation:

7.4.4. This measure should be implemented from the start of the Belgian Plan for Rare Diseases. A deadline of 12 months seems feasible. The FAMHP could be in charge of the implementation and of the supervision of the ethics committees.

Aspects related to costs:

7.4.5 There is no budget impact on the health insurance system.

Measure 7.5. Academic (non-commercial) clinical trials for rare diseases should be stimulated financially and made more visible

Issue addressed:

7.5.1. Not all academic (non-commercial) clinical trials are reported and registered. This is a general phenomenon in Belgium and not specific to rare diseases only. In the case of rare diseases the impact is however bigger because of the small number of patients, the life-threatening aspect, and the absence of alternative treatments. Transparency on clinical trials can therefore have a high impact and should be pursued.
There are several barriers that explain this situation:

- the increased cost of doing clinical trials, as they have to be compliant to Good Clinical Practice (GCP) and GMP/GLP (Good Manufacturing Practices and Good Laboratory Practices, respectively);
- many researchers do not know when their research falls under the scope of the clinical trial Directive or in the scope of the Belgian Law of 7 may 2004 (experiments on the human being);
- many researchers are not well informed on the European advanced therapy medicinal products (ATMP) regulation[67] which is important when they develop potential therapies on the basis of tissue engineering, cell therapy or gene therapy.

67 http://eur-lex.europa.eu/LexUriServ/site/en/oj/2007/l_324/l_32420071210en01210137.pdf

Academic clinical trials may be a source of creating new knowledge and finding new treatments. Knowledge about which trials are on-going and which results they obtained, whether positive or negative, can help other teams in other countries in advancing towards a treatment. Many of these trials are based on the use of drugs 'off-label'.

Description of the measure:

7.5.2. **The combination of three actions:**

- **awareness raising at the level of researchers / investigators;**
- **an adapted approach for adherence with GXP standards (cost-effective manner);**
- **making the information on on-going clinical trials available to different stakeholders (linked to measure 7.1 above)**

Alternative and complementary measure:

A fund should be created to co-finance academic researchers who invest in clinical trials for rare diseases or, more generally, to cover unmet medical need.
This could be a public fund or a PPP.[68]

Expected impact:

7.5.3. More transparency, which should lead to better decisions at different levels (regulatory authorities to individual patient) and reduced barriers for performing clinical trials by academic sponsors, which should lead to more drugs/therapies reaching the market in the long run.

Aspects related to timing and implementation:

7.5.4. This proposed measure could be implemented from the start of the future Belgian Plan for Rare Diseases.

Aspects related to costs:

7.5.5 There is no budget impact on the health insurance system. We estimated that costs are linked to the communication plan and the training and education action towards the academic sector. The cost price for the setup of a support program for academic clinical studies is included in area 9.

More information on budgetary aspects is included in annex 8.

68 *Public private partnership*

Measure 7.6. The role of the Special Solidarity Fund should be clarified.

Issue addressed:

7.6.1. The Special Solidarity Fund (SSF) is a last resort for patients to get reimbursement of medical treatments in cases where their life is at risk and there is no alternative treatment available under the provisions of the health insurance. The functioning and the efficiency of the Special Solidarity Fund were recently assessed by the Belgian Health Care Knowledge Centre.[69]

Although the situation can vary greatly year by year, in practice, more than half of the funds of the SSF are used for the reimbursement of drugs prescribed for the treatment of rare diseases.

Initiatives like the one proposed for early temporary access of orphan drugs mentioned below should reduce this burden by creating a mechanism that is part of the normal process and would guarantee a more equal treatment of patients.

Still, there are other issues related to the functioning of the SSF that need clarification to ensure that the SSF fulfils its role as it has been meant by the legislator. These issues include:

- the SSF is sometimes used to reimburse individual patients who are part of compassionate use or medical need programmes;
- the present legislation is ambiguous for orphan drugs for which a college[70] exists: can an individual patient still request the Fund's reimbursement if they are not meeting the criteria as defined and applied by a College?;
- can the SSF be used to reimburse cohorts of patients with a rare disease and not only individual patients;
- costs charged to the patient are at the moment not part of the maximum contribution rule. It is not clear whether this is a policy or the consequence of the exceptional nature of the SSF;
- the same applies to the turnover of pharmaceutical companies: SSF reimbursements are apparently not taken into account for quota calculations.

Description of the measure:

7.6.2. **Clarification of the SSF remit should be pursued particularly on:**

- **the possibility of the SSF to intervene on reimbursement decisions for drugs where a college exists. The recommendation being that the SSF could intervene for indications not covered by the college that was established, thus for other indications than the ones mentioned in the criteria for reimbursement;**
- **transparency and the obligations of physicians to report on efficiency of the treatments**.

Expected impact:

7.6.3. More transparency, which should lead to better decisions and more equity for individual patients.

Aspects related to timing and implementation:

7.6.4. This measure is rather technical and can necessitate changes in legislation. Clarifications can probably be achieved within a 12 month timeframe.

69 *Optimisation of the operational processes of the Special Solidarity Fund, KCE reports vol.133C, http://www.kce.fgov.be/index_en.aspx?SGREF=9470&CREF=16772*

70 *For slightly more than half of the orphan drugs that obtained reimbursement in Belgium, a college is established who is in charge to advise Insurance companies on individual reimbursement decisions.*

Aspects related to costs:
7.6.5 It can be expected that the proposed measure will have an impact on the budget if the recommendation concerning the interpretation of the current legislation is followed. However, this impact is difficult to estimate as we are dealing with 'exceptional' cases. Therefore, a budget estimation is not foreseen for this proposal.

More information on budgetary aspects is included in annex 8.

Measure 7.7. Ensure that materials for compounding used to treat rare diseases, can be used legally.

Issue addressed:
7.7.1. Various materials for compounding are at the moment used to treat rare diseases but for some, this use is currently not legal in Belgium, because these materials need analysis certificates to comply. To avoid for the benefit of the patient, that a de facto illegal practice needs to be continued as there is no alternative treatment available, which implies responsibilities and risks for hospital pharmacists, the proposal is to entrust the suggested Platform for Rare Diseases with the task to ensure such materials for compounding are identified and that they are transmitted to the appropriate authorities and/or organisations for analysis in order to obtain the adequate certificate for human use. These instances should also analyse the possibility that such materials are integrated on the reimbursement list.

A list of 19 substances has been prepared as part of the preparation of these recommendations and proposals for the Belgian Plan for Rare Diseases (see addendum 5). In collaboration with the FAGG/AFMPS, the suggested Platform for Rare Diseases could develop a mechanism to regularly update the list of materials for compounding which should undergo the certification procedure.

Description of the measure:
7.7.2. **Give the FAGG/AFMPS and/or the proposed Platform of Rare Diseases the authority and or the means to organise the control and certification of batches of the approved substances so that they can be used legally by pharmacists**.

Expected impact:
7.7.3. The benefit to the patient is a certainty of continued treatment with a legal basis. It also improves the safety of the treatment for the patient.

Aspects related to timing and implementation:
7.7.4. The FAGG/AFMPS installed a working group on this subject that will review the list of raw materials and also develop validated compounding procedures (Therapeutisch Magistraal Formularium/Formulaire Magistrale Thérapeutique) used for the treatment of patients with rare diseases.

Aspects related to costs:
7.7.5 The budgetary impact is small, but a budget should be made available to ensure that the analysis is performed on each batch, and certificates can be made available.
This may be covered by an annual budget for miscellaneous expenses of 10.000 Euro.
More information on the budgetary aspects is included in annex 8.

Measure 7.8. Setting up a system for early access to orphan drugs including early temporary reimbursement.

Issue addressed:

7.8.1. Orphan drugs go through two different processes before they actually reach the patient. When the pharmaceutical company considers the drug is ready to be introduced on the market, it applies for a Marketing Authorisation (MA) through an EU-level procedure. After this MA is granted, it will then approach the different Member States to obtain decisions as to the reimbursement of the drug. Patients have access to the treatment only when the drug is reimbursed. This two stage process means it can take years between the moment of application for MA and the moment when a Belgian patient has access to the treatment.
Taking into account the characteristics of rare diseases, this often means no access at all as the patient might not live anymore when the drug eventually becomes available. This potential measure is only applicable for new drugs that cover unmet medical needs.

Description of the measure:

7.8.2. **The proposed measure is to create an early access for patients to cover unmet medical needs through new (orphan) drugs through a system of Early Temporary Access (ETA) and Early Temporary Reimbursement (ETR)**: at the time a marketing authorization application (MAA) is introduced at the European Medicines Agency, the pharmaceutical company (sponsor) can apply for an Early Temporary Access (ETA)/Early Temporary Reimbursement (ETR) with the Belgian authorities[71]. The authorities will review the ETA/ETR fast taking medical need and available evidence into account. When the ETA/ETR is granted, an agreement is signed including the commitments of all parties under the ETR. The ETR will stop when marketing authorisation is refused or withdrawn, or when normal national reimbursement enters into force or is refused. A risk-sharing plan will be part of the agreement.

This proposed measure concretely implies:

1. To install a multi-stakeholder Working Committee, under the joint responsibility of INAMI/RIZIV & FAGG , with, if appropriate the scientific regulatory advice of EMA to evaluate a high unmet medical need to conditionally authorize a product for early temporary authorization (ETA) and decide on the conditions of early temporary reimbursement (ETR) as described in working document of WG 5
2. To continue to ask advice from this Working Committee during each milestone in the whole procedure of the official reimbursement that may start as from positive opinion of the Committee in charge at EMA (CHMP).
3. Treating physicians should be requested to fill in real life clinical added value patient data (CAVOD) through a therapeutic register as from the start of the early access until the revision, that can be consulted by the agreed upon parties, in order to avoid duplication of work.
4. The revision at national level should take the EMA revision timelines into consideration.

Expected impact:

7.8.3. The impacts for the patients are:

- Belgian patients would get access to the drug at least 12 months faster than what is now the ideal situation, and probably 18 to 24 months faster than the present average time period;
- a secondary impact is that industry will be encouraged and incentivised to develop more orphan drugs as

71 During the application for ETR, provision by the sponsoring company of products as CU for those patients for which ETR is applied for is mandatory for the whole application period, estimated to be 3 months.

they will be reimbursed faster, and will also be motivated to install more compassionate use and medical need programs in Belgium, allowing faster access to treatment to patients.

Aspects related to timing and implementation:

7.8.4. An initiative is under implementation as part of the measures included in the Cancer Plan, as well as on the basis of proposals made in the Recommendations and Proposed measures for a Belgian Plan for Rare Diseases – Phase 1.

Aspects related to costs:

7.8.5 The budgetary impact of the measure is difficult to estimate, as it depends on the actual behaviour of the pharmaceutical companies. The system should make Belgium more attractive allowing to introduce medicines faster to the market.

Taking into account the experience up to now with orphan drugs and the expectation that approximately 10 new drugs would enter the market each year, this measure 'could' generate an increase for the orphan drugs budget of 5 to 10 million Euro/year (or 8 to 15 % taking 2008 as a basis). This would be a one-off extra cost. For the implementation of the initial steps to allow earlier access and reimbursement for certain pharmaceutical products or innovative therapies off label or not yet marketed nor reimbursed, a budget of 3.5 million Euro has been provided in the 2011 budget by the General Council of the RIZIV/INAMI. This budget is a recurrent cost for the total duration covered by these proposals, i.e. 5 years.

Measure 7.9. Colleges for orphan drugs have proven to be a good practice. Their role and use could be enhanced and strengthened for a higher impact.

Issue addressed:

7.9.1. At the moment of deciding on the reimbursement of a new orphan drug, the Minister of Social Affairs and Public Health can decide to set up a 'college' for the indication for which the reimbursed drug is approved. This is being done for approximately half the orphan drugs approved and has proven to be a good practice.

The Colleges role is to advise the Medical Advisor of the insurance organism who has to take the decision for individual patient reimbursement. These colleges therefore look at individual patient cases and verify whether the patient's situation corresponds to the criteria for reimbursement. In practice, all decisions related to orphan drugs are referred by all insurance organisms to the Colleges, leading to a build-up of expertise.

Description of the measure:

7.9.2. **The proposed measure is to enhance the role of the Colleges through a set of measures**:

- to strengthen the remit of the Colleges by adding in the appreciation that the College also takes into account the degree of therapeutic evidence in function of the individual situation of the patient;
- to implement the recommendation made in a KCE report on orphan drugs to create a single entry point for individual reimbursement applications;
- to strengthen the administrative support to the Colleges in order to cope with the expanded remit and number of drugs;
- to consider to involve the Colleges as advisors to the CTG/CRM during the analysis of a demand for reimbursement of a new drug. This will also improve and enhance their present role of proposing revisions to the criteria defined by the CTG/CRM.

Expected impact:
7.9.3. Enhanced Colleges should lead to faster decisions for individual patients.

Aspects related to timing and implementation:
7.9.4. Implementation can start immediately after launching the Belgian Plan for Rare Dsieases, probably through the setting up of a working party to advise the RIZIV/INAMI in reforming the Colleges.

Aspects related to costs:
7.9.5 This measure will cost through the fees that have to be paid to experts participating in Colleges and through the costs for the administrative support and the single entry point. These costs should be higher with the proposed enhanced role than they are at the moment but an estimation is currently not possible. The costs will be part of the budget of RIZIV/INAMI.

More information on the budgetary aspects is included in annex 8.

Measure 7.10. Responsible off-label use of drugs should be possible to treat patients with rare diseases under specific conditions

Issue addressed:
7.10.1. Off-label use is the term used for the treatment of patients with a drug for an indication or under conditions that are not mentioned in the conditions of the marketing authorisation. Off-label can mean use for a different indication, but also a different age category (typically children) or even dosage.
Off-label use of orphan drugs is limited due to the cost of these medicines. But off-label use for these expensive drugs can appear through medical need programmes or at the level of the SSF as mentioned above.
Off-label prescription is a general phenomenon for medicinal products, and can in some instances be of great interest for the patient. In the case of rare diseases, it even can be beneficial as a solution for patients for whom no alternative treatment exists.

Off-label use creates problems for all parties involved:
- prescribers feel they are limited in their therapeutic freedom to treat their patients in high need and are taking risks as they carry the responsibility;
- authorities are concerned that use outside the approved conditions might lead to safety and other risks;
- insurance authorities doubt whether they should reimburse treatments that have no proven efficacy;
- patients are reluctant to sign comprehensive 'informed consent' forms.

Description of the measure:
7.10.2. **The proposal is to regulate the off-label use for rare diseases under specific conditions**:
- when no better therapy is available for the rare disease;
- when a scientific basis and general (international) consensus exists on the use of this drug for the indication;
- when a complete clinical follow-up is kept (efficacy, safety,…);
- when this information is reported to a central authority (e.g. the FAGG/AFMPS) that regularly evaluates and take measures if necessary. In the case of rare diseases, this reporting can happen via the National Registry;

- reimbursement of such off-label use can be obtained if all the above conditions are fulfilled and should be possible under the SSF. It can be imagined that the SSF and RIZIV/INAMI may want to use for such decisions the expertise which is available in the Colleges;
- Belgium should propose to collaborate at EU level about off-label use of rare disease treatments.

The existence of a National Registry and a network of Centres of Expertise as proposed in these recommendations and measures for the Belgian Plan for Rare Diseases, would make the implementation of the proposed measure feasible.

Expected impact:

7.10.3. The main impact is more patients that will have access to novel treatments using off-label drugs. With the proposed measure, the information on the on-going treatments will circulate better among practitioners as will information on the efficacy.
Authorities and health insurance will benefit through the higher level of transparency and reduced uncertainty under which decisions are taken.

Aspects related to timing and implementation:

7.10.4. Implementation can start immediately after the launch of the future Belgian Plan for Rare Diseases, and after working out the notification modalities and the criteria for reimbursement, by advertising this policy towards the medical community and the patients' organisations.

Aspects related to costs:

7.10.5 The potential budgetary impact of this measure is very difficult to estimate. The fact off-label use becomes more transparent does not necessarily mean the cost to the health insurance budget will be higher. Better treatment should lead to savings in the long run. On the short term, however, this proposed measure will lead to more request at the level of the SSF. Therefore, a gradual increase up to 1 million Euro/year was included in the budget proposal, despite the many uncertainties.

More information on the budgetary aspects is included in annex 8.

Measure 7.11. Support home treatment for orphan drugs under clear conditions.

Issue addressed:

7.11.1. The treatment regime of orphan drugs is often simple but may be required over a long period of time and adherence by the patient may be an issue. Reimbursement of an orphan drug treatment is now nearly always linked to a treatment in hospital setting (although not necessarily by the hospital pharmacist who obtained permission). Home treatment may substantially improve adherence and the patients' quality of life. If set up appropriately it can be a safe and acceptable alternative for ambulant hospital treatment. Patients for whom home treatment would be an option must be able to make their own informed choice between hospital-based and home treatment.

Description of the measure:

7.11.2. Concrete measures proposed include:

- for oral forms of orphan drugs, it could be examined whether and to which extent they can be dispensed by the community pharmacist for home treatment;
- parenteral orphan drugs with cytotoxic properties should always be prepared in the safety cabinet of a hospital pharmacy and administered in a hospital setting;
- other parenteral orphan drugs (including ERTs, …) must be prepared and administered in the center of reference /center of rare disease for the considered rare disease at the start of treatment. Follow-up therapies may be prepared in a hospital pharmacy near the patient's home and administered at home by a trained home nurse;
- for home treatment with orphan drugs, patients should have the possibility to access home care services to administer such treatment. The prepared orphan drug would be collected at the hospital pharmacy and delivered, at a time agreed upon with the patient, at his/her home. The hospital pharmacist is responsible for storage, handling and compounding of the ready to use orphan drug. The community pharmacist may supply additional material such as sterile needles, syringes, antiseptic solutions etc.
- all home treatment activities are performed under the responsibility of the treating physician at the Centre of Expertise/Coordinating Centre of Rare Disease. An agreement about such home treatment would need to be signed by all parties involved (nurse, hospital pharmacist, community pharmacist, recognised service provider, treating physician and patient) which included a treatment protocol and a product specific manual which is based on the SmPC (product leaflet).

Expected impact:

7.11.3. The benefits are mainly for the patient and relatives. These benefits are significant both in terms of economic value (e.g. savings on travel, less loss of working time) as in quality of life for the patient.

Aspects related to timing and implementation:

7.11.4. Implementation can start after the Centres of Expertise are recognised and are made aware of the policy and apply it.

Aspects related to costs:

7.11.5 Budget impact: home treatment is expected to be cost-neutral to slightly less costly than hospital treatment.

More information on the budgetary aspects is included in annex 8.

Measure 7.12. Stimulate patient adherence through a set of initiatives.

Issue addressed:

7.12.1. Patient (non-)adherence to treatment is an as major issue for orphan medicines as it is for other medicines. Because rare diseases are life-threatening and/or seriously debilitating and often have a high treatment cost, patient adherence for orphan drugs should be monitored and appropriate measures installed. This should be addressed at different levels: the patients, the physician, the pharmacist, the patients' organisations and the industry.

It is expected that better adherence will lead to better treatment and lives saved, and that costs will mostly be linked to setting up the measure itself.

Description of the measure:

7.12.2. Concrete measures proposed include:

- that patient adherence data could be systematically collected at the pharmacy level with the ambition to improve patient adherence for oral orphan medicines. The gathered information should be systematically transmitted to the treating physician on a patient-by-patient basis and not only in general statistics to allow the physician to act. For the implementation of this measure, aspects of data privacy, safety and optimal use of IT tools should be considered;
- communicate better to physicians and patients about why patient adherence to treatment for a life-threatening or seriously debilitating disease is important. This should also be linked when appropriate to home treatment as proposed in measure 7.11.;
- the consequences on reimbursement in case of long-term lasting non-adherence should be investigated and principles should be set up and communicated to the involved parties as part of the communication and information;
- (EU-level): Adherence for oral orphan medicines can also potentially improve by a more adapted packaging of a medicine. Because product packaging is approved at EU level, it is proposed to conduct a study at the EU level on how to best stimulate adherence through adapted packaging and how to stimulate on that basis good practices for industry and how to integrate such package-related patient adherence information in the label of the medicine by regulatory authorities;
- (EU level) Post-marketing trials should also record patient adherence. Registries for rare diseases may be a good tool for this. Outcomes based on non-adherence should be collected as well. Therefore, it is recommended that EMA includes patient adherence aspects appropriately in its requirements for post-marketing trials and registries.

Expected impact:

7.12.3. It is expected that better adherence will lead to better treatment and lives saved.

Aspects related to timing and implementation:

7.12.4. Implementation can start with the launch of the Belgian Plan for Rare Diseases but timing can be slightly different depending on the different sub-measures.

Aspects related to costs:

7.12.5 Budget impact: costs will mostly be linked to setting up the measure itself or are part of the budget of the proposed communication plan (measure 4.4.). An increase in adherence will lead to higher costs to the health insurance budget, but these costs were foreseen at the moment of taking the reimbursement decision.

More information on the budgetary aspects are included in annex 8.

Measure 7.13. Belgium to take a leading role in a number of European issues related to access to treatment for patients with a rare disease

Measure 7.13.1. Belgium should promote the revision of the EU Clinical Trials Directive and make sure a series of improvements are included in it.

Issue addressed:

7.13.1. Some of the measures mentioned above are linked to the present EU Clinical Trials Directive. A process is on-going to revise this Directive which is the occasion to improve it in order to better meet the specific needs of clinical trials for rare diseases with a very limited number of patients.

These improvements are linked e.g. to:

- harmonisation and efficiency of reaching decisions. Multiplication of procedures are costly and in the case of rare diseases can lead to simply not starting a clinical trial as the costs can never be recuperated due to the limited market size. Different measures mentioned above try to tackle this issue: the voluntary harmonised procedure should become an harmonised procedure; a single ethics committee opinion at EU level is of course better than achieving this at Belgian level;
- the application of the Helsinki Declaration with regards to the rights of patients who participate in clinical trials in case the trial is stopped, should be clarified and integrated. The present situation, is as mentioned above, not satisfactory;
- registration of clinical trials as a source of information for experts and patients should be mandatory.

Description of the measure:

7.13.2. **Belgian authorities should ensure that expert knowledge acquired through the implementation of the Belgian Plan for Rare Diseases is used to improve the EU Clinical Trials Directive so that it meets the specific needs for clinical trials on rare diseases**.

Expected impact:

7.13.3. More transparency, which should lead to better decisions at different levels (regulatory authorities to individual patient) and better protection of patients.

Aspects related to timing and implementation:

7.13.4. This measure is linked to the timing of the revision of the Directive. Implementation should start with the launch of the Belgian Plan for Rare Diseases and can take the form of a specific working party under the umbrella of the suggested Platform for Rare Diseases and under the presidency of the FAGG/AFMPS.

Aspects related to costs:

7.13.5 There is no budget impact on the health insurance system.

Measure 7.13.2. Belgium should propose to change the criteria used to grant orphan designation when appropriate materials for compounding are available and used.

Issue addressed:

7.13.6. The COMP has granted orphan drug designation to products although a material for compounding (so called 'raw materials') may be readily available on the European market, which could be used for treatment of a specific rare disease. When such designated products reach the market as orphan drugs, they do encounter

difficulties to obtain reimbursement as a much cheaper alternative exists in the form of a material for compounding.

Description of the measure:

7.13.7. It is therefore recommended that the **European Commission avoids that efforts are made to develop orphan drugs which will risk not to be reimbursed based on the price difference with the existing material for compounding, taking the benefits of the orphan medicine versus the material for compounding into account**. Specifically, it is asked that the COMP reviews article 3.2 of the Regulation EC141/2000 about whether such materials for compounding should be included under the definition of 'existing treatment'.

Measure 7.13.3. Belgium to take a leading role to boost EU-level initiatives in relation to early Marketing Authorisation, early reimbursement and more efficiency in monitoring after Market Authorisation.

Issue addressed:

7.13.8. The proposed system for early temporary reimbursement, should ideally be set-up at the EU level. That may lead to a parallel examination and decision for marketing authorisation (at EU level) and for reimbursement (at the Member State level). In the framework of these recommendations, it is proposed that the European Commission works out an EU-wide proposal for early temporary access (and reimbursement) for orphan medicines and to link the collection of treatment data to this access.

Both the EU level at the moment of market authorisation, and the National level, at the moment of reimbursement decisions, take the initiative to organise or impose data collection to monitor the clinical efficacy of the drug. This is nearly always the case for orphan drugs as decisions are most often taken on limited clinical information due to the lack of patients.
These initiatives are at the moment not standardised and not coordinated. This leads to an abnormal burden on both industry and clinicians and could be organised more efficiently.
The discussions that are presently on-going about the EU-level collection of clinical added value data about orphan drugs (CAVOD)[72] is linked to earlier access as well.

Description of the measure:

7.13.9. **Belgium could take a leading role to improve the efficiency of the whole decision-making process. Present initiatives at the level of a coordinated exchange of clinical information as mentioned above should be pursued as they can lead to faster reimbursement decisions and avoid the present duplication**.
But more initiatives are possible and needed to avoid unnecessary costs and delays.
The proposed system for Belgium, with a parallel decision on access and reimbursement, could be Europeanised as mentioned above.
Coordination with regard to setting up registries and timing of revisions of decisions between the EU (market access) and national (reimbursement) levels are obvious.

72 *Improving access to orphan medicines for all affected EU citizens, Final Conclusions and Recommendations of the Pharmaceutical Forum, page 4, bullet 'Exchange of knowledge amongst Member States and European authorities on the scientific assessment of the clinical added value of orphan medicines.', http://ec.europa.eu/pharmaforum/docs/pricing_orphans_en.pdf*
and EAHC-tender 'The creation of a mechanism for the exchange of knowledge between Member States and European authorities on the scientific assessment of the clinical added value for orphan medicines', http://ec.europa.eu/eahc/health/tenders_H05_2010.html

Expected impact:

7.13.10. EU-level cooperation and harmonisation will lead to better earlier access for patients, and decisions and significant savings through a higher efficiency and cost sharing.

Aspects related to costs:

7.13.11. This measure should not generate direct budgetary impacts and in the longer term, only net savings. It does however imply continued attention at policy level and resources to actively participate and eventually lead EU level initiatives.

Measure 7.13.4. More transparency is needed on the use of medical devices to treat patients with rare diseases.

Issue addressed:

7.13.12. There is a need to better understand and document the use of medical devices such as implants, surgical procedures and other medical and paramedical acts to treat rare diseases. Based on such better understanding, improved rules for use, control and reimbursement can be developed.

This issue is particularly relevant for devices being applied in the body of patients. These implants are often categorised as 'experimental'. This may lead to loss of transparency or notification to authorities and to circumvention of the use of a CE label. This leads to questions about responsibilities of prescriber, pharmacist and authorities towards the patient.

Implants are also at the centre of ethical debates, including on equity of access depending on capacity to pay.

Description of the measure:

7.13.13. Concrete measures proposed include:

- reimbursable access to medical devices, surgical implants and procedures and other important medical or paramedical acts to treat or care for rare disease patients, should be documented. It is suggested that the Belgian Federal Agency KCE would evaluate how an inventory can be set up for non-CE marked devices and implants along with a reporting obligation about their use for the hospital pharmacists. Further measures should be proposed, based on such inventory, to optimize use and reimbursement.
- (EU level) These issues should be compared at European level and Belgium should be involved or take initiatives in preparing EU recommendations for these issues.

Expected impact:

7.13.14. It is expected that this will lead to improved patient safety and more cost-effective use of these devices.

Aspects related to timing and implementation:

7.13.15. Implementation can start with the Plan. More concrete measures could be foreseen to be taken at a mid-term evaluation of the Plan.

Aspects related to costs:

7.13.16. There is no direct impact on the health insurance budget.

Area 8. Comprehensive care of the patient

Patient testimonials

"To avoid risk of infection, doctors advised us to wait before putting the child into crèche. I had to give up any idea of returning to work. It was a very difficult time and the loneliness, both socially and intellectually, was hard to bear."

"M. has metachromatic leukodystrophy. If she got pneumonia, it could be fatal. The fear of infection forced us to take her out of school as of September 2010. A court case is ongoing to validate this decision. But while awaiting the outcome of that, our family allowance has been stopped. The health insurers will not pay for a childcare worker or home help. All they can offer is a carer for a maximum of 10 days per year!"

"Adapting our home for the child's condition cost us €80,000. The AWIPH (Agency in Wallonia for integrating people with disabilities) gave us a grant of €16,000."

"With this type of illness (metachromatic leukodystrophy), there is a never-ending amount of paperwork to fill in (most recently related to absorbent products for the purpose of incontinence). Nobody tells you about the administrative updates that you have to do. You have to know about them and think of them yourself. For the health insurers, rules are rules regardless of whether it is an exceptional situation brought about by a rare disease."

"In the end, my mother had to give up work to look after my father. Her own health suffered as a result. He required a lot of care. For example, you had to feed him while ensuring that he didn't choke or vomit. At one point, the costs were reaching €285 per month which was a lot at the time. Even the special products for feeding him, which were quite expensive, had to be paid for by us."

"Every five years, patients must go before the consulting doctors. It is an unnerving, difficult, humiliating and inhumane experience which can have negative psychological effects. Some patients go as far as to stop taking their medication a week before to prove that they are genuinely ill."

Introduction

8.1. Adapted social services are instrumental to the empowerment of people living with rare diseases and improve wellbeing and health. For people living with a rare, chronic and debilitating disease, care should not only be restricted to medical and paramedical aspects, but should also take into account social inclusion, psychological and educational development.
In this regard, many patients with a rare disease can benefit from measures which are taken in the Programme for Chronic Diseases.

Supporting documents:
The proposals in this area were elaborated by the working group responsible for working package 2: 'Comprehensive care for the patient'. This working group has drawn up a supporting document. This document can be can be consulted on the webpage of the Fund Rare Diseases and Orphan Drugs (supporting documents) via www.kbs-frb.be.
The supporting document submitted by this working group, like all other supporting documents, has not been validated by the Management Committee of the Fund.
Furthermore, annex 6 includes a number of guidelines which should facilitate the implementation of this proposal.

Measure 8.1 To simplify the access to measures concerning diagnosis and coordinated treatments, to propose the assistance of a 'care coordinator'

Issue addressed:
8.1.1. For a long time the management of patients with a rare disease was in Belgium random and not fully guaranteed for every person. A simplification of the access to diagnostic measures and access to coordinated treatments must reduce the current existing discrimination between people with a disease. Not everybody receives the proper amount of adapted treatments, materials, and help. Although some of the rights are already existing, they are not always known by their potential beneficiaries.
The purpose of this measure (and of measure 8.2) is to enable to people suffering from rare diseases to receive, like all other people with a disease, a global answer adapted to their needs. It would also help to fill the current lack of management of these needs (see also annex 6).

Description of the measure:
8.1.2. The passage through a Centre of Expertise is strongly recommended to the people suffering from a rare disease. This recommendation includes that people can have recourse to other specialised care facilities as well: a Centre for Human Genetics or to other specialised 'consultants' (i.e. external experts, specialized in these diseases, and who can be in a network with the Centre). The follow up of the patient can also be assumed by a specialized practitioner, networking with the Centre (see also measures in area 1).

8.1.3. **It is the purpose of this measure that the Centre of Expertise will propose for some diseases or group of diseases a medical, paramedical and social roadmap of patient management. For the patient, that comprehensive roadmap should simplify the current situation**.

8.1.4. **In each Centre, patients should have the possibility to be advised and receive support from a care coordinator**. This coordinator simplifies and eases the roadmap of the patient, including the administrative procedures patients have to go through to exercise their rights. Care coordinators provide them with the necessary information, they are the link between the patient and all the medical, paramedical or psychosocial stakeholders. They also favour the link between the Centre and the network developed by the Centre, but also the links with local care services, peripheral specialists, GPs, patients' organisations, sickness funds, other Centres and with all administrations involved in the medical and social status of the patient.
The care coordinator is also responsible for the mobilization of the rights of the patients (see measure 8.2).

8.1.5. **The Centre takes into consideration the global needs of the person. It registers the patients, and determines their individual needs by a complete check-up, which includes the diagnosis and the stage of the disease, but also adds a functional diagnosis (CIF)**. The Centre formulates a therapeutic pathway and decides about the possible opening of (social) rights for the patient (see measure 8.2).
The Centre will pay attention to inform the patients about new developed treatments or new clinical trials concerning their diseases.
The Centre proposes an organizational help, adapted to everyone. Its services are conceived to answer the specific needs of each patient.
If the expertise in not available in a Belgian CE, the Centre refers the patient to an expert or a Centre abroad, with the help of the care coordinator.

Expected impact:
8.1.6. With the help of the care coordinators, patients will be better informed about their disease, its evolution, its transmission, its treatments, with an opening toward their other needs and the social consequences of their diseases. They will get access to the network created by the Centre or linked to the Centre (Patients Associations, local network;…). If needed, they'll be oriented to a Centre of reference abroad.
The planned system allows a global management of the patient, including the not strictly medical need. The patient roadmap and the access to all information needed to better manage their disease, will be easily accessible: the care coordinator will play an important guiding role.

8.1.7. Integration of medical and nonmedical networks between various stakeholders will provide a comprehensive and integrated service to patients.

Aspect related to timing and implementation:
8.1.8 This global management and this roadmap of care should start progressively with the installation of the Centres. They'll start disease by disease.

Aspects related to costs:
8.1.9. With the majority of tasks being linked to the number of patients, the financing of the function of the care coordinator is proposed to be calculated based on the number of patients treated within the Centre. Hospitals having only one CE, should therefore consider cooperation with nearby hospitals to ensure the function is taken up in cooperation.

8.1.10. For all CEs together, including patients followed in CEs outside Belgium, the budget estimate for the fifth year, after full implementation of the future Belgian Plan for Rare Diseases, is 8,8 million Euro. The actual reimbursement cost would be monitored using timesheets, comparisons between CEs and benchmarking. The value would be revised annually based this monitoring and on good practice.

More information on the budgetary aspects are included in annex 8.

Measure 8.2. To facilitate the access to specialized help, to simplify the administrative procedures

Issue addressed:

8.2.1. The presence of a rare disease does not inevitably imply the presence of specific or unique symptoms, treatments, required material, or social consequences. But these, very often more general, symptoms, treatments, needs strike attention because of their acuteness, their intensity, their difficulties to be managed in the day-to-day life and their impact on the quality of life and life expectancy.

8.2.2. Surveys performed by Patients' Associations, as the testimonials of patients included in this document, strongly show the existing lacks in the management of the patient with a rare disease as much as for the needs for materials or other needs linked to a special, very often, 'unknown' disease. For some patients, their disease indeed implies specific needs, related to its rarity.

8.2.3. It is both possible and desirable to make up for the inequality originating from rarity and to meet a number of needs currently not covered by a legislation which doesn't take into account the specific needs of this category of users. The goal of this measure is to bring these 'weak users' at the same level of rights as all other users and to provide an answer responding to their specific needs.
It costs the patients a huge amount of energy and time to obtain the recognition and the access to their rights. Not everybody is able to face these challenges, and the result can be that social injustice is added to the weight of the disease.
This measure (as well as measure 8.1) must enable every patient to benefit from already existing rights, but it must also provide an answer to specific individual needs, without heavy administrative procedures.
A more extended and comprehensive representation of this proposed measure is included in annex 6.

Description of the measure:

8.2.4. **The proposal is to simplify the exercise of rights by patients with a rare disease to paramedical treatment, materials, products, devices, subsidies, care and help,…. Or these rights already exist, or they could be included in new and specific listings if they answer specific needs for which there has not been taken care of at this moment. These listings should be elaborated for a single rare and severe disease or for a group of diseases**.

This proposed measure contains three separate issues:

1. In function of a specific rare disease (or a group of rare diseases) the specific needs of the patients should be identified and coupled to existing interventions to which the patient is entitled. This identification of needs allows the care coordinator to give the patient correct and updated information about his rights (social rights, financial compensations, treatments,…, where and how to obtain them,…). Patients will be better informed and will easier have access to their entitlements.
   Specific needs and requirements can be identified, with support of the Platform for Rare Diseases and/or the Advisory Council of the Observatory for Chronic Diseases, in collaboration with other actors (CEs, patients' organisations,…).

2. In function of a specific rare disease (or a group of rare diseases) the needs and requirements of the patients should be identified for which there are no interventions or compensations to which he/she is currently entitled to. Or these rights might be allocated to patients with another pathology (with similar symptoms and needs), or these rights are not existing in the current legal and administrative context.
   These specific needs and requirements can be identified, with support of the Platform for Rare Diseases and/or the Advisory Board of the Observatory for Chronic Diseases, in collaboration with other actors (CEs, patients' organisations,…).
   The information on the identified needs and requirements should be passed on to the competent authorities (e.g. the Scientific Council of the Observatory for Chronic Diseases, and others). These authorities can objectively analyse these needs and eventually formulate solutions by allocating supplementary rights (enlarge the target group who can benefit, adapt the criteria, create new interventions and rights,…). This analysis will include a budgetary impact analysis. Furthermore, a distinction have to be made between rights and compensations which fall within the health insurance covered by RIZIV/INAMI (medical acts, drugs,…) and interventions and compensations for which other authorities and ministers are responsible. In the latter case, RIZIV/INAMI can transfer this information/questions to the Minister of Social Affairs and Public Health who can discuss this further with his/her colleagues ministers.

3. Finally, there is the identification of existing rights and interventions for which an administrative simplification is possible (e.g. through an argued paper by a medical specialist from a Centre of Expertise or a Liaison centre, without the need of an intervention from a Medical Advisor from the sickness funds).

Following these principles, it should be feasible to objectify the needs of patients with specific rare diseases and to gradually satisfy (a number of) their needs. One should be aware, however, of the existing limited budgetary possibilities and the health and social priorities with regards to the needs of other people should be taken into account.

8.2.5. The lists with needs/requirements and rights will be 'continuous work in progress': they will be regularly reviewed and completed, by the same procedure as for their elaboration.

8.2.6. The final decision of the allocation of new rights will be taken by RIZIV/INAMI, after consultation with the involved CEs and after consensus with other competent authorities. It is important that decisions are taken on the basis of equity and fairness.
In addition, the political structures (federal, regional or at community level) involved in the measures which are proposed in the lists, will have to give their approval. Then, if needed, they will have to adapt their regulation to enable the application of these new rights.
The RIZIV/INAMI and competent structures could collaborate and cooperate in a common working group. Attention will be paid to the fact that the decisions or answers of the concerned authorities will be taken within a reasonable amount of time.

8.2.7. For the patient:
- practically, the Centre directly notifies the sickness fund the diagnosis (categorical and functional) and the therapeutic plan of the patient;
- the Medical Advisor 'flags' the patient;

- if the patient enters into the required criteria, this 'flag' opens the access to the rights included in the list connected to his disease, without any other administrative procedure. The patient is informed by his sickness fund that he will be able to benefit the rights depending on his own needs and the fixed criteria.

8.2.8. For the Centres:
- with the help of the evaluations realized by the Centre, the Centre will only open the benefit of rights for the patients for whom the situation justifies such a possibility (stage of the disease, respect of the criteria of Chapter IV, etc.);
- the Centre will collaborate in a systematic and closed way with the patient network (GP, physiotherapists, nurse, specialist of reference, etc.), and to promote shared care.

8.2.9. For the sickness fund, the RIZIV/INAMI and others stakeholders:
- the sickness fund pursues a posterior control to check that the benefit of the rights was granted based on the needs of the person and with respect to specific criteria corresponding to the needs included in the list of the disease;
- the RIZIV/INAMI and the Inter-Sickness funds Agency will monitor the global expenditures, by pathology and by Centre;
- the electronic transmission of data and the creation of a unique standardized file for the providing of the different types of help are planned;
- the system will be evaluated thanks to the data provided by the Centre to the registries, the Sickness Funds, the Inter-Sickness funds Agency, the Associations of Patients, the Observatory for Chronic Diseases and the Platform for Rare Diseases. A global analysis of these data, realized for example by the Institute of Public Health, will be focused on the cost/health ratio, the functioning of the Centres, the collaboration and the functioning between networks. Taking into account these evaluations, adjustments can be provided;
- with the help of the Observatory for Chronic Diseases, attention will be paid to ensure that each administrative structure involved in the roadmap of the patient will simplify its procedures, for example by avoiding non necessary requests or useless renewals.

Expected impact:

8.2.10. For the patient, this system becomes simple, without administrative hurdles. The establishment of listings allows to provide the benefit of the rights depending on individual needs and taking into account their evolution.
The system becomes transparent and more equitable.

8.2.11. The Centres and providers are rendered responsible. Control on this responsibility is performed 'a posteriori'.

8.2.12. All of the authorities concerned by the disease and its impact have to collaborate.

8.2.13. The framework of the roadmap care of patients enables to add progressively new approaches, discoveries and new answers to needs.

Aspect related to timing and implementation:

8.2.14. The elaboration of the specific needs can start from the installation of the Centres.

Aspect related to costs:

8.2.16. Some administrative savings are expected at the level of the sickness funds. The management of specific needs or not encountered needs until now will have a certain cost. In some cases, the measures and the rights provided by the listings will only concern a few or a limited number of people. However, taking into account the diversity of rare diseases combined with the variety of specific needs, every extension of rights should be accompanied by a careful and sound budgetary impact analysis. Decisions should take the available budgetary space into account.

Area 9. Stimulating research on rare diseases

Patient testimonials

"There has been progress. Some treatment is a lot more effective. A couple who lost their 18-year-old daughter said to me a few years ago, "you're part of the lucky generation". However, the massive hope that has been put in research has not yet been fruitful. Yet time passes and patients' quality of life diminishes as a result of the illness."

"Every day, my daughter was losing some of her capacity.... walking, speaking etc. I was frightened by the speed with which it happened. Yet no treatment – except comfort – can be given for this illness."

Introduction

9.1. The best way to increase our knowledge on rare diseases in general is through research, both basic research and clinical research. Research on rare diseases is scattered throughout the EU and it is comparatively scarce with respect to the high number and heterogeneity of rare diseases. The recent methodological and scientific advancements provide new and powerful approaches that can be used to reveal the mechanisms of many rare disorders. However, various reasons make research on rare diseases difficult to conduct.[73]

9.2. Research into rare diseases can be beneficial for society as a whole. Since most rare diseases result from a dysfunction of a single pathway due to a defective gene, understanding the impact of this defect may yield insights into more complex and multifactorial pathways in common diseases. Therefore, stimulating research into rare diseases leads to scientific breakthroughs in frequently occurring disorders (i.e. the case of homozygous familial hypercholesterolemia which led to the development of statins, or genetic research on the hereditary forms of Alzheimer's disease and Parkinson's disease have led to the elucidation of the presenilines/APP-pathways and parkin pathways respectively which are now being further investigated for drug development,…).

9.3. Research on rare diseases has also been a driver for innovation. Rare diseases were instrumental for human genome mapping and gene cloning during the 90s and at the beginning of this century, and today extensive exome and full genome sequencing projects on DNA from patients with a rare disease are highly successful.
Also the involvement of pharmaceutical and biotechnological industry in developing new treatments for rare diseases is steeply increasing. Currently 20% of all innovative products obtaining a marketing authorisation in Europe are developed for a rare disease.

9.4. With 63 orphan drugs approved at EU level and with approximately 800 orphan drug designations, a specific treatment is not yet available for most rare diseases, though. So, the unsatisfactory situation of the available treatments of rare diseases is evident. European and national initiatives in the field of rare diseases are therefore necessary to foster basic biomedical research and translational research for the development of orphan drugs and other effective treatments for rare diseases. It is also important to develop research in non-pharmacological treatments, e. g. rehabilitation, surgical treatments and medical devices.

73 *Recommendations for the development of National Plans for Rare Diseases, Guidance document, EUROPLAN, p. 36, http://www.europlanproject.eu/public/contenuti/files/Guidance_Doc_EUROPLAN_20100601_final.pdf*

9.5. A number of measures proposed in other areas, have a direct impact on the stimulation of research on rare diseases. These include for example the mandatory condition that Centres of Expertise should be involved in fundamental, translational, and clinical research on rare diseases. Furthermore, area 7 includes a number of measures to stimulate clinical research and clinical trials on patients with a rare disease.

9.6. The proposed measures on basic and translational research in this document originate from a 'Research Forum' organised by the Fund of Rare Diseases and Orphan Drugs which took place in Brussels on January 28, 2011. This Forum was attended by scientists, medical doctors, research managers, representatives from the cabinet, health administration and research sponsoring organisations (like the FPS Health, Food Chain Safety and Environment; RIZIV/INAMI; FWO; FNRS) and from patients' organisations. Other measures come from the working groups.

Supporting documents:
Minutes of the 'Forum on Rare Disease Research in Belgium' which took place in Brussels on 28 January 2011 can be consulted. [The link will be activated when the Recommendations and Proposed measures for a Belgian Plan for Rare Diseases will be published].
This report is a supporting document submitted by the working group that organised the Forum. Just as all other supporting documents, this document has not been validated by the Management Committee of the Fund.

Measure 9.1. Research projects on rare diseases should be made identifiable and traceable within (national) research support programs

Issue addressed:
9.1.1. There are many clinical academic and non-academic researchers who are dedicated to basic research on rare diseases. But most often this research is not labelled as rare disease research because it is supported through general financing channels for biomedical research. This makes inventorying research on rare diseases difficult, leading to a decrease in the visibility of this research.

Description of the measure:
9.1.2. **All Belgian research funding agencies, like FWO, FNRS, IWT, universities…, are requested to 'label' all research projects on rare diseases in the future so that they can be easily included in the appropriate databases (like Orphanet)**.
Since nowadays most submissions for research grants are done electronically, it is suggested to add an extra 'thick box' on the submission forms indicating whether a submitted proposal for a research project or a research mandate applies to rare disease or has an impact on a rare disease.
This implies that the agencies need to have a good working definition on what a rare disease is, or alternatively, they should be able to refer to a list with all recognised rare diseases (this could be the Orphanet list and, in the future, ICD-11).

Expected impact:
9.1.3. Making research projects on rare diseases identifiable and traceable, and including information on them in the proper databases (like Orphanet), would increase the visibility of rare disease research and of the research groups involved.

This could be an information instrument for patients and result in easier access to diagnostic and therapeutic expertise and to take part in research projects (basic, translational and clinical).

Aspects related to timing and implementation:

9.1.4. FWO and FNRS already agreed that they would investigate this possibility for their future research calls. They would make the information available to the appropriate body. This could be the Belgian Orphanet team at WIV/ISP or the Platform for Rare Diseases.

The Belgian Orphanet team and/or the Platform for Rare Diseases should take contact with other research sponsoring organisations asking them to implement this measure.

Aspects related to costs:

9.1.5. There are no direct costs involved. Costs for follow up of this measure fall under the responsibility of the Platform for Rare Diseases and Orphanet Belgium (for the extraction of data and adding them into Orphanet).

Measure 9.2. Increase national support to E-rare

Issue addressed:

9.2.1. E-Rare is a program supported by the European Commission ERA-Net scheme, first under the Sixth Framework Program (2006-2010) and today under the Seventh Framework Program: E-Rare-2 (2010-2014). E-Rare-2 (ERA-Net on rare diseases) is a network of sixteen partners – public bodies, ministries and research funding organizations – from twelve countries, responsible for the development and funding of national/regional research programs on rare diseases. E-Rare fosters research on rare diseases in Europe and associated countries. E-Rare partners systematically exchange information on rare diseases research and organise joint funding initiatives.

Both FNRS and FWO are partners in E-Rare and have made budgets available to support research programs from Belgian scientists submitted during E-Rare-2 Call 2011 on 'Transnational Research Projects on Rare Diseases'. This call closed on January 31, 2011.

The interest to participate in the E-Rare-2 program of – excellent – Belgian rare disease research groups in both sides of the country was very high. It should be realised, however, that both FNRS and FWO will each support only one project in this call with a budget of approximately 200.000 euro. The selected projects will be the best ranked Flemish and French Belgian project, respectively.

9.2.2. Although E-Rare is supported by national funding, it fosters networking at EU level. International networking is an important factor for success in rare disease research. Moreover, since projects are evaluated according to EU standards, by international specialists in the field of rare diseases, the selection will be rigorous and only the best research projects will be ranked favourably.

Description of the measure:

9.2.3. The participants to the Research Forum and the members of the Fund for Rare Diseases and Orphan Drugs recommend that **a larger part of the regional research budgets will be allocated to E-Rare, resulting in the support of more than two projects at Belgian level**.

Expected impact:
9.2.4.The support to collaborative, high quality research on rare diseases will be increased. This should in the long run benefit patients for whom there is currently no appropriate treatment.

Aspects related to timing and implementation:
9.2.5. Preferably this measure will be implemented in the next upcoming call for projects at E-Rare.

Aspects related to costs:
9.2.6. There are no direct costs to the healthcare budget since the financing involves a transfer of existing research funds towards E-Rare.

Measure 9.3. An impulse program for research on rare diseases

Issue addressed:
9.3.1. Research on rare diseases is difficult to conduct, for various reasons: the high number and wide variety of the diseases, the lack of suitable experimental models for most rare diseases, the poorly defined endpoints, the small number of patients and, above all, the limited resources. Such difficulties are especially relevant to the development of translational research, which is necessary to bridge the gap between basic research and therapy development. Clinical studies on rare diseases, which are of high added value, may also need complex collaboration among EU countries since the number of patients enrolled and the amount of data collected in a single country may not be enough to draw statistically significant conclusions about the efficacy of the treatment under investigation. Finally, public health and social studies on rare diseases and patients' needs are limited and these issues have received attention only recently.

9.3.2. Research project proposals on rare diseases are often granted a lower priority by experts in the selection committees of funding agencies because it is assumed that the research outcomes are beneficial to only a limited number of patients.
This discrimination is not justified because it is based on misconceptions. In fact, new scientific data revealed by research on rare diseases in humans are often relevant for understanding human biology, which is beneficial for rare and common diseases in the long run. In addition, basic research on rare diseases can provide direct input for translational research and the development of new diagnostic tools and therapies with a great impact on the life quality of the individual patient (e.g. enzyme replacement therapy). Funding agencies and their experts should be made aware of this high impact of research on rare diseases in human health care.

Description of the measure:
9.3.3. Because of these reasons, **the Federal Minister of Public Health is asked to launch a federal impulse program for funding research on rare diseases, comparable to the research program that was initiated at the instigation of the Cancer Plan. Such a stimulation program would be limited in time**.

Expected impact:
9.3.4. An impulse program would make research on rare diseases more visible; give researchers on rare diseases the opportunity to intensify their research and bring it up to the standards they can apply for other national or European funding programs; give an incentive to high level research groups to enter into the field of rare diseases.

In the long run, this intensification of research will benefit the patient.

9.3.5. A similar impulse program for research on rare diseases was part of the first French Plan for Rare Diseases. The program was very successful: it gave French research on rare diseases a boost, forced individual groups to form national research networks, and groups that were supported by this program, significantly increased their success rate in general funding calls at national and European level, later on.

Aspects related to costs:
9.3.6. An investment of 9 million Euro in research for a programme implemented over a the full period of the future Belgian Plan for Rare Diseases is recommended.

More detailed information on the budgetary aspects is included in annex 8.

Measure 9.4. Identification of unmet medical needs

Issue addressed:
9.4.1. Policy makers do not have at their disposal objective information as to the unmet medical needs of patients with a rare disease. Such an inventory, and the identification of priorities within this inventory, is not readily available, but would be needed to steer policy making and decision-making.
One of the potential initiatives announced at the Ministerial Conference on innovative medicines organised by the Belgian EU Presidency in October 2010 was to realise such an inventory.

Description of the measure:
9.4.2. The measure proposed is that Belgium would actively promote and participate in the realisation of a study aimed at inventorying unmet medical needs, ensuring that rare diseases are an integral part in it and that the specificities of rare diseases are taken into account to ensure they receive the appropriate attention. Without this assurance, they risk to be wiped out, exactly because of the rarity of the disease and the low impact in terms of number of patients.

Expected impact:
9.4.3. An objective inventory of unmet medical needs would allow the identification of priorities in health and social care and a subsequent adaptation of the policy. This would benefit the patients with the highest needs. The objective identification of unmet medical needs allows for a more equitable distribution of the scarce resources.

Aspects related to costs:
9.4.4. There are no direct costs involved.

Measure 9.5. Public funds available for translational research in rare diseases

Issue addressed:

9.5.1. At the moment, public funds are available for translational research, but developments of treatments for rare diseases compete with more common diseases. They have little chance to obtain funds because of the selection criteria used (i.e. the way impact in calculated).

Description of the measure:

9.5.2. A solution to solve the difficult access for translational researchers on rare diseases could be to earmark part of the current funding specifically for rare diseases. Another solution would be to create a public private partnership (PPP) to invest in the development of new treatments.

Expected impact:

9.5.3. Translational research has the aim to speed up the process of treatment development and reducing the barriers for performing clinical trials. Especially in the case of rare diseases, this could be an approach which could lead to more drugs/therapies reaching the market in the long run.

Aspects related to costs:

9.5.4. An investment of 3 million Euro is recommended as a minimum.

More detailed information on the budgetary aspects is included in annex 8.

Area 10. Management of the future Belgian Plan for Rare Diseases

Introduction

10.1. The Fund for Rare Diseases and Orphan Drugs recommends that the future Belgian Plan for Rare Diseases should be implemented into the general health and social care system in a sustainable way. The various proposed measures should, as far as possible, be assigned to existing structures within the current health and social care system.

10.2. Nevertheless, the overall process of implementing optimized global care to patients with a rare disease, and to coordinate registering, information provision, networking and research on rare diseases, an organisational structure specifically dedicated to rare diseases, is indispensable.

10.3. The lack of such a single managing organisation appeared to be one of the weaker points of the French Plan for Rare Diseases 2005-2008.[74] The dispersion of tasks and responsibilities over various authorities and the alternate presidency of two governmental agencies over the 'Comité de pilotage' – leading to a lack of common vision – had a negative impact on the dynamic of the French Plan.
For the new term of the French Plan, the recommendation was made to have an effective control structure in place[75] with political legitimacy and the authority of permanent monitoring, evaluation, coordination and adjustment.

Supporting documents
The 'Evaluation of the French Plan / Evaluation du Plan national maladies rares 2005-2008', [link: http://www.hcsp.fr/docspdf/avisrapports/hcspr20090317_maladiesRares.pdf] which was published in April 2009, is considered by the members of the Fund to be an important and inspiring document for their recommendations in this domain.

Measure 10.1. Creation of a Platform for Rare Diseases

Issue addressed:
10.1.1. The practical implementation of the proposed measures needs to be coordinated since many stakeholders and governmental agencies are involved.

Description of the measure:
10.1.2. It is proposed to **create a Platform for Rare Diseases to assist the Minister of Social Affairs and Public Health in the implementation of the measures that he/she will propose in the future Belgian Plan for Rare Diseases. Possibly, the Platform for Rare Diseases could function in a similar way as the Cancer Centre which was set up in September 2008 after a convention between RIZIV/INAMI and WIV/ISP, during the launch of the Cancer Plan**.

74 *Haut Conseil de la santé publique, Évaluation du Plan national maladies rares 2005-2008, April 2009, p.60.*

75 *Haut Conseil de la santé publique, Évaluation du Plan national maladies rares 2005-2008, April 2009, p.65.*

10.1.3. The main assignment of the Cancer Centre is to inventory, advise and evaluate. It facilitates the collaboration between the actors, evaluates the efforts in the battle against cancer and advises on the basis of the collected expertise from the field and scientific data.[76]
The members of the Fund for Rare Diseases and Orphan Drugs recommend that in a similar way, the Platform for Rare Diseases functions as:

- an advisory body for the concerned health authorities: the Minister of Social Affairs and Public Health, the various administrations (RIZIV/INAMI, FOD/FPS,…), involved institutes (WIV/ISP,…) and other structures (Colleges,…). The Platform for Rare Diseases will advise on the best possible way to implement the future measures that will be proposed and decided upon by the Minister and that will make up the future Belgian Plan for Rare Diseases;
- an evaluating organisation that would coordinate the mid-term (after 3 years) and final (after 5 years) evaluation of the outcomes of the future Belgian Plan for Rare Diseases;
- a facilitating organisation that would be the engine of the various networking and collaborating initiatives which are necessary to turn the future Belgian Plan for Rare Diseases into a success.

10.1.4. The Platform for Rare Diseases will have a number of tasks. These tasks are summarised in the list below, but this list is non-exhaustive:

- advise the governmental organisations that manage the selection of the new Centres of Expertise and on the centres constituting the LRD (measures 1.1. and 1.3.);
- participate in the yearly reviews of the functioning of the CEs and the activities of the centres belonging to the Liaison network for Rare Diseases. It mainly concerns the facilitation of the networking process within and between the CEs, the CHGs and the LRD, including passing on best practice and suggesting improvements (measure 1.1, 1.3., 1.4.);
- monitor the functioning of the Liaison network for Rare Diseases in the University Hospitals and their partnerships with CEs and CHG (measure 1.3.);
- monitor the networking activities between CEs and peripheral care services (measure 1.5.);
- follow up of the regular customer satisfaction evaluations performed at level of CEs and the cooperation of CEs with patients' organisations (measure 4.2.);
- accompany the various working groups and act as their secretariat (i.e. working groups to support measures (non-exhaustive list):
  - ◇ 1.3. development of care and therapeutic pathways;
  - ◇ 4.3. collaboration between patients' organisations;
  - ◇ 5.1. teaching of professionals;
  - ◇ 6.2. access and reimbursement for non-DNA tests;
  - ◇ 7.7. materials for compounding;
  - ◇ 7.10. off-label use;
  - ◇ 7.11. home treatment;
- facilitate the implementation of measure 8.2 (this could lead to the creation of specific working groups, but not necessarily);
- ensure the liaison with the various stakeholders, which includes the preparation of the decision-making process and the monitoring of the implementation of decisions taken. This includes decisions linked to launching calls for new CEs, the definition of care and therapeutic pathways (measures 1.1. and 1.3.);

76 *Kankerplan: Stand van zaken, maart 2011, p. 67, http://www.laurette-onkelinx.be/articles_docs/20110323_-_SVZ_Kankerplan.pdf*

- follow up of the staff in charge of communication and the management of the communication plan, including the coordination of the four main components and the cooperation with stakeholders, particularly the patients' organisations (area 3);
- follow up of the the evaluations;
- follow up of the national and international networking;
- collaborate with the relevant governmental bodies (incl. the Minister, administrations and relevant experts in EU organisations) on the establishment of the proposed measures 7.13.;
- interact with various grating bodies at national and international level to boost research (fundamental, translational, clinical) on rare diseases (measures in areas 7 and 9);
- work together with the neonatal screening centres since these centres are a cornerstone in the early screening and detection of many rare disease patients;
- monitor the development (and if necessary implement) of a medical passport for patients with a rare disease (measure 4.4.);
- organise regularly exchanges including training sessions for staff of Centres of Expertise. This is particularly important for the care coordinators (measure 8.1.) and liaison officers (measure 1.3.) as these are new functions;
- …
- …
- …

10.1.5. The Platform might be directed by a Board composed of representatives of all relevant stakeholders and governmental organisations involved in rare diseases, depending on the mission given to the Platform. In any case, the members of the Board of the Platform will be appointed by the Minister.

10.1.6. To perform the above mentioned functions, it is proposed that the Platform would have a staff of at least four FTE (manager, senior professional, junior professional, organisational assistant):

- one of these persons would be a secretary general. This person should act as the manager or secretary general of the Belgian Plan for Rare Diseases;
- another member of the team should be a communication specialist to manage the communication plan, the portal website and cooperation agreements with stakeholders related to communication objectives;
- the three staff members who would assist the secretary general
  - ◇ can be hired (full time or part time);
  - ◇ likewise they can be seconded from existing authorities/institutions (this is the case for the new term of the French Plan);
  - ◇ or their tasks can be covered through service contracts with third parties.

Independently of this choice, the economic cost will be similar and is included in the budget of the Plan.

10.1.7. In order to carry out its various tasks, the management of the Platform for Rare Diseases can be assisted by specific working groups of experts and stakeholders with dedicated tasks dealing with specific issues.

Expected impact:

10.1.8. The major impact of this measure on patients and other stakeholders is that there would be an official steering platform which would deal with all aspects of rare diseases.

Aspects related to timing and implementation:

10.1.9. The Platform should be created at the start of the Belgian Plan for Rare Diseases.

Aspects related to costs:

10.1.9. For the Platform for Rare Diseases four types of costs should be taken into account:

- salary cost of staff – 400.000 Euro/year;
- working costs of staff and of functioning working groups – 170.000 to 270.000 Euro/year. In this budget a number of supporting tasks for various proposed measures are foreseen. A large part of this budget will be used for the setting up and running of the evaluation panels for the CEs and the regular revision of the care trajectories (medical and financial dimensions);
- evaluation of the Plan in the third and fifth year – estimated at 500.000 Euro;
- a budget of 30.000 Euro/year is earmarked to develop and provide ad hoc training programmes for staff of the network of CEs, CHGs and LRD.

More detailed information on the budgetary aspects is included in annex 8.

Area 11. Ethics and governance

Introduction

11.1. On 22 February 2011 the Fund for Rare Diseases and Orphan Drugs organised, in collaboration with the Belgian Advisory Committee on Bioethics and the patient alliance RaDiOrg.be, the colloquium 'Care and cure for Rare Diseases: societal and ethical aspects' (Zorg bij zeldzame ziekten: maatschappelijke en ethische aspecten/ Soins relatifs aux maladies rares: aspects sociétaux et éthiques).
Besides a discussion of the European and Belgian initiatives concerning the care for patients with rare diseases, the specific needs of patients and the procedures concerning the development and the access to orphan drugs, the emphasis of the colloquium was on the contribution of the society to the costs for rare diseases and on societal solidarity. Questions are e.g. at what moment solidarity is in conflict with the limited resources of our health care system? When is a specific treatment becoming too expensive to be taken up by health care systems which are based on the solidarity principle? How can/should policymakers make difficult choices in allocating scarce resources and budgets to patients with specific diseases?
These questions arise in health care in general, but are even more relevant concerning rare diseases. Treatments for rare diseases (medicinal and other) are often expensive and the part of the health care budget devoted to rare diseases is increasing. Is their a limit to this increase? Can rarity in itself be a reason to claim a greater share of the societal solidarity? Can or should other criteria be implied?
The symposium triggered two measures to be proposed for the Belgian Plan for Rare Diseases.

Supporting documents
The proposed measures in this area are inspired on the colloquium 'Care and cure for Rare Diseases: societal and ethical aspects' organised by the Fund on 22 February 2011 in Brussels. A report of this colloquium can be consulted on the webpage of the Fund Rare Diseases and Orphan Drugs (supporting documents) via *www.kbs-frb.be*.

Measure 11.1. Transparency on the price setting of orphan drugs

Issue addressed:
11.1.1. Given the increasing availability of orphan drugs and their often high price, decision makers are faced with an increasing proportion of pharmaceutical expenditure being spent on orphan medicines. To date, little is known of the factors affecting pricing of orphan medicines. Although pricing of orphan medicines follows the same economic logic as medicine pricing in general, specific for orphan medicines is that:

- substantial R&D and manufacturing process costs need to be recuperated while only a small number of patients are treated;
- orphan drugs benefit from a period of marketing exclusivity following marketing authorisation;
- few alternative health technologies target the same rare disease;
- in most EU member states orphan drugs are exempt from providing cost effectiveness data for reimbursement;
- third-party payers and patients have limited negotiating power;
- orphan drugs are often amongst the most innovative;
- often no other treatment exists as a comparator.

Although these conditions apply to some orphan medicines, it should be emphasised that they do not apply to all approved orphan medicines.

11.1.2. The subject is mainly linked to the cost for society: although the number of patients is limited, the high average cost of treatment leads to a noteworthy proportion of available resources that go to this type of medicines. During the colloquium of 22 February 2011 this issue appeared as critical.

Description of the measure:

11.1.3. Price setting of orphan drugs by Pharmaceutical companies is an European, even global issue. The current scientific literature on the matter does not reveal any immediate solutions.
Ideally, an independent health technology assessment organisation at EU level (i.e. one or several members of the EUnetHTA network)[77] should investigate to what extent normal price setting rules apply (or not) to orphan drugs; what the costs and the risks are which are born by the developers; what the official point of view is of each of the main stakeholders in relation to the price setting of orphan drugs; to what extent the prices of orphan drugs differ between EU member states; and which potential mechanisms can increase the transparency in price setting of orphan drugs?
In case a study at European level is not feasible, a similar study could be performed by the Belgian Health Care Knowledge Centre (KCE)[78].

11.1.4. The objective pursued by the study should be to identify routes to increase the transparency of price setting, as this would open up a way to facilitate the process of decision-making from market authorisation to reimbursement. Also at EU level, in the framework of the CAVOD project (Clinical Added Value of Orphan Drugs), studies are on-going concerning improved decision-making processes between national and European authorities, based on clinically added value of the orphan drugs.

Expected impact:

11.1.5. For the patient
Since orphan drugs on the Belgian market are fully reimbursed, the direct impact for the patient is limited. However, one can expect that with a smoothed process of reimbursement decisions, more orphan drugs will become sooner available to the patients.

11.1.6. For other stakeholders
More openness and transparency on price setting of orphan drugs could facilitate the decision making process at the level of EU and national authorities, would ensure reasonable price settings without eroding the eagerness of the industrial partners to invest in the development of new innovative treatments for patients with a rare disease.

Aspects related to timing and implementation:

11.1.7. Deadlines for study proposals submitted to KCE is usually at the end of April for the year program of the next year.

Aspects related to costs:

11.1.8. There are no direct costs involved when the study proposal is taken up by the KCE or the European Commission.

77 *European network for Health Technology Assessment, EUnetHTA, www.eunethta.net/*

78 *Belgian Health Care Knowledge Centre, www.kce.fgov.be*

Measure 11.2. Citizens' consultations on rare diseases and orphan drugs

Issue addressed:

11.2.1. Making difficult health care policy decisions, for example on cost-effectiveness of health care interventions, requires judgement based on scientific arguments (scientific value judgement) and what is good for society (social value judgement). The scientific evaluation of cost-effectiveness is in itself already very difficult but can be approximated by currently accepted methodology. In regard to the social value judgement, much has still to be done, e.g. concerning the question who should advise the decision makers.

To solve this issue, the UK National Institute for Clinical Excellence (NICE) establishes Citizens' Councils to provide NICE with an insight into the social values that the public might display when given the opportunity to deliberate on the issues facing the Institute.[79] Each social value judgement by the Citizens' Council is based on the opinion of a group of approximately 30 citizens who:

- examined the available evidence (normally presented by documentation and a series of expert witnesses);
- deliberated on this evidence (both by questioning witnesses and debating within the Council) in order to produce logical and defensible conclusions.

The members of the Citizens' Council are ordinary members of the public, representing the UK. In this way, the policymaker in the UK wants to ensure that the views of those who fund the National Health System - the public – are incorporated into the decision-making process.

11.2.2. For the reimbursement of (ultra-) orphan drugs the NICE Citizens' Council issued an advice after a three day deliberation in November 2004.[80] An exempt of the advice reads as follows:

> "The majority (20 out of 27) of Citizens' Council members came to a conclusion that it is sometimes, or always, justified for the NHS to pay premium prices for ultra-orphan drugs. For twenty of us, the NHS should vary its normal assessment of cost effectiveness to allow expenditure on ultra orphan drugs where necessary.… For sixteen of us, rarity on its own is not a factor – the degree of severity must come into the picture.…"
>
> [The full report: *www.nice.org.uk/niceMedia/pdf/Citizens_Council_Ultraorphan.pdf*]

11.2.3. Recently, an EU wide (EUROBAROMETER) survey reveals that Europeans have a relatively accurate understanding of what rare diseases are but detailed knowledge and awareness remain low. The European public expresses strong support for policy initiatives linked to rare diseases at both national and European level, and Europeans see the actions of allocating resources to improve research, ensuring access to care and raising awareness as highly justified.[81]

Description of the measure:

11.2.3. **It is advised that on a number of pending ethical and societal issues [on rare diseases and / or orphan drugs] a mechanism is installed to properly ascertain the public's opinion. Social value judgements derived from a citizens' deliberation in the form of a citizens' conference, a citizens council or any other in-depth participative consultation procedure could be helpful for the policymaker to make appropriate decisions on these matters**.

79 *Citizens Council, National Institute for Health and Clinical Excellence, National Health System, www.nice.org.uk/aboutnice/howwework/citizenscouncil/citizens_council.jsp*

80 *NICE Citizens Council Report, Ultra orphan drugs, London, November 2004, www.nice.org.uk/niceMedia/pdf/Citizens_Council_Ultraorphan.pdf*

81 *European awareness of Rare Diseases, Special Eurobarometer 361, http://ec.europa.eu/health/rare_diseases/docs/ebs_361_en.pdf*

It might be worthwhile to install a mechanism of citizens' consultations in a larger framework of health care assessments and not exclusively focused on rare diseases and orphan drugs.

Expected impact:

11.2.4. Impact on the patient

A citizens' consultation is different from a patients' consultation. During such a consultation, the citizens form a cross section of the population (not necessarily a fully representative cross section, but the section should at least bring to surface the diversity of major opinions in the population). Moreover, the citizens are often more distantly related to the topic compared to patients. Therefore, not all advices formulated during a citizens' consultation will necessarily be in accordance with the stakes of the (individual) patients.

11.2.5. Impact on other stakeholders

Citizens' participation is an emanation of democracy. Public involvement gives policy makers a sense of their constituents' fears and hopes. It exposes the values and norms which are living among the public, and thus indicate the public response to a particular ethical or societal issue. Public consultation can guide policymakers towards more motivated and wider accepted decisions.

Aspects related to timing and implementation:

11.2.6. It could be a task for the suggested Platform for Rare Diseases to organise at least one citizens' consultation on specific ethical, societal and policy issues concerning rare diseases and/or orphan drugs during the first five years of its instalment. With its broad expertise in participatory consultations, the King Baudouin Foundation[82], the organisation managing the Fund for Rare Diseases and Orphan Drugs, could be a partner in the organisation of these consultations.

In case other governmental or semi-governmental organisations involved in health care assessments and/or health care policy (like RIZIV/INAMI, KCE, WIV/IPH, FPS Health, The Advisory Council for Bioethics,…) would be organising such consultations, the Platform could put specific topics concerning rare diseases on the agenda of those discussion forums.

Aspects related to costs:

11.2.6. Organising such citizens' consultation is a cost, both in terms of staff time, physical costs, reimbursements paid to the participants, facilitation, reporting, translations, etc. If the suggested Platform gets the responsibility to organise such a citizens' consultation, this would have implication in the need for staff and in a budget for management of the process. This cost is estimated at 75.000 Euro for each cycle.

More detailed information on budgetary aspects is included in annex 8.

82 www.kbs-frb.be

4. TIMING OF THE IMPLEMENTATION, MONITORING AND EVALUATION

4.1. The Fund for Rare Diseases and Orphan Drugs suggests that, on the basis of the proposed measures in this document, the implementation of the future Belgian Plan for Rare Diseases will be a gradual process over a timeframe of 5 years. This is not only the time needed to progressively implement the proposed measures, but also to generate critical mass and momentum, and to be able to measure the impact. The necessary investments are also spread over a period of 5 years.
The aggregate of the proposed measures is building upon the existing systems and provisions within the Belgian health care system. As indicated in the next chapter on the impact of the budget, the Belgian authorities are already investing heavily in the treatment of people with a rare disease. The aim of the proposed measures is to give a boost to the efficiency of the patient management, to reach more patients and to increase the impact of the sharing of knowledge and resources with other countries.

4.2. The members of the Fund propose that the Platform for Rare Diseases should play a central role in the evaluation and monitoring of the implementation of the future Belgian Plan for Rare Diseases.
The dimension 'timing, monitoring and evaluation' of the future Belgian Plan for rare diseases should be further developed by the competent authorities in collaboration with this proposed Platform for Rare Diseases. But a few principles need to be clear:

- the regularity of meetings of the Board of the Platform is considered a necessity for proper monitoring;
- the Platform should create a separate working group in charge of evaluation. This working group should define the evaluation process and steer it. It should regularly review the targets, deadlines and achievements, and report back to the Platform, the Minister and other involved governmental bodies;
- this working group should clearly make the difference between monitoring and evaluation. A budget is proposed to be available to the Platform to contract an external evaluator to assist in a mid-term and final evaluation. Monitoring on the other hand should be a permanent task embedded in the implementation, allowing the feedback on a regular base to the management organ of the Platform of facts and figures on the implementation compared to expectation;
- the central stakeholder of the Belgian Plan for Rare Diseases is the patient. Patient opinion and satisfaction should be part of any evaluation exercise;
- the Platform should produce a yearly report on the advancement of the Plan;
- when creating separate working groups, the Platform should each time clearly define objectives, targets and responsibilities;
- working groups in charge of specific measures should also be in charge of regularly reviewing indicators, or defining new indicators whenever relevant.

4.3. Two tables in annex 7 give a first not validated overview of potential targets and indicators for the success of the measures proposed by area. The first table compares the proposed measures for Belgium with indicators proposed by the Europlan project. The Europlan project has defined indicators which can be used by all EU Member States. Therefore, the first table allows to evaluate which areas are covered and which not by the Recommendations and Proposed measures for a Belgian Plan for Rare Diseases, in comparison to the European recommendations.
The second table comprises proposals for indicators. Also these indicators are inspired by the Europlan project. But on the long term, the proposed Platform for Rare Diseases should collaborate at European level to elaborate a best practice and – if possible – to develop 'health outcome indicators'. For the moment, such health outcome indicators were not part of the Europlan project.
The proposed indicators should be validated by the working group responsible for the evaluation of the future Belgian Plan for Rare Diseases, as indicated above. A definitive set of indicators could then be proposed to the Minister together with the first year report.
The table below, and the indicators, should be considered as a starting point, together with the Europlan outputs and material that would become available at EU level in the future. It is important to develop the indicators based on EU-level consensus as this will help to compare results among countries.

4.4. Benchmarking
The Eurobarometer survey commissioned by the European Commission and conducted at the end of 2010, provides an interesting benchmark concerning the situation in Belgium before the launch of the future Belgian Plan for Rare Diseases. One can expect that the European Commission will conduct a similar survey in a number of years, which will make it possible to measure the impact of the investments in Belgium and in other European countries.
De Eurobarometer has questioned the general public only. Likely, this public is not well informed on the subject. It would be useful to conduct a similar survey (as benchmarking) among medical professionals, both in first and second line. Preferably, this would also be conducted at European level in order to allow comparison between countries. If, however, this is not organised at EU level, it is recommended to conduct such a survey in Belgium during the first year of the implementation of the Belgian Plan for Rare Diseases (in any case before the major investments have happened). Part of the budget on evaluation could be used for this.

5. ANALYSIS OF THE IMPACT ON THE BUDGET

5.1. The proposed measures in this document will have an impact on the budget of the authorities, mainly on the budget of the health care insurance. This impact can occur under the form of savings, as well as increasing expenditures.
The budgetary impact was calculated for each proposed measure separately. The document clarifying these calculations, is included in annex 8. In this chapter, the general budgetary impact of the proposed measures is summarized. The estimation is performed as if all proposed measures would be implemented 'en bloc'. Although this scenario might be unlikely, one should realise that some measures will have a different cost and impact if they are not implemented in combination with other proposed measures.

The expenditures for rare diseases today

5.2. One of the key ambitions of the proposed measures is to increase the efficiency of the care system for patients with a rare disease. The major impact obtained by these proposed measures is:

- an improved service of care and patient management;
- more equity;
- cost savings, at the level of the health care insurance as well as the personal budget of the patient and his relatives, as a consequence of an improved efficacy of the care and patient management.

These savings will be realistic, without doubt, but they will be difficult to calculate. Moreover, they will be negated by additional expenditures which will be generated.

5.3. It is important to realise that the Belgian health care system is already investing in rare diseases today:

- There are the expenditures associated with the reimbursement of orphan drugs. Orphan drugs are – per definition – used to treat persons with a rare disease. Although the number of patients is relatively low, the expenditures are significant. It is estimated that in Belgium 80 million Euro were spent in 2010. We can expect that the budget for orphan drugs will increase in the future. Some of the proposed measures in this document might have the effect that this increase will be slowed down. These are measures concerning transparency of price formation at EU level, the combination of decisions on market authorisation and reimbursement, the setup of registries, the collection of data on clinical effectiveness, the control of the use of drugs used off-label, etc.
- The financing of the current Reference Centres for Rare Diseases (metabolic diseases, cystic fibrosis and neuromuscular diseases) by a convention (contract) with RIZIV/INAMI. During 2010 the current budget was estimated at 6 million Euro for the treatment of 3.000 to 3.500 patients. The transformation of these centres, form their current contractual basis, to Centres of Expertise, as foreseen in proposed measure 1.1., will not result in extra expenditures.

- The financing of the 8 Centres for Human Genetics. Approximately 80% of the patients for whom a diagnostic test is being performed at the Centres for Human Genetics are patients with a rare disease. The budget of the CHGs for 2010 was approximately 70 million Euro.

Creating a momentum – in investment of 17 million euro over a period of 5 years

5.4. The measures which are proposed in this document, contain a one off investment of 17 million Euro over the whole period of implementation.

The investments are necessary in order to:

- give the research on rare diseases an impulse (12 million Euro);
- create a National Registry for rare diseases coupled to disease specific registries (2 million Euro);
- organise communication campaigns towards different target groups to make the network of Centres of Expertise and the Liaison network widely known and to improve the awareness on rare diseases in the general population and among the professional caregivers (1,7 million Euro);
- organise evaluations 3 and 5 years after the initial implementation of the future Belgian Plan of Rare Diseases (0,5 million Euro).

Expenditures for the improvement of the quality of life of patients with a rare disease – 156 million Euro over a period of 5 years

5.5. Many of the proposed measures induce regular – mostly yearly – expenditures. We expect that the yearly recurrent budget will rise to approximately 44 million Euro from the fifth year onwards of the implementation of the Belgian Plan for Rare Diseases.

The largest part of this budget is linked to 2 measures:

- the setup of Centres of Expertise (measure 1.1.);
- the function of the care coordinator (measure 8.1.).

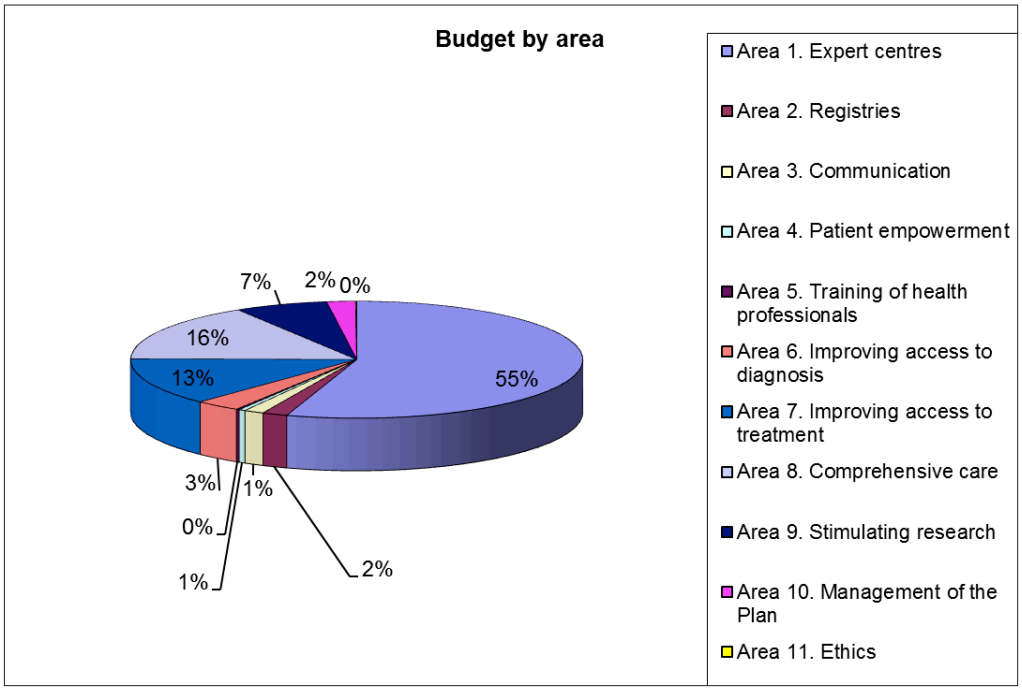
Both measures together represent 75% of the recurrent expenditures.

The starting point of this estimate is that from 2016 onwards, approximately 18.000 patients with a rare disease will be diagnosed and treated in specialised and recognised Centres, on top of the patients who already have access to such Centres. Again, the proposed estimates assume that all measures will be included in the future Belgian Plan for Rare Diseases and be implemented. A scenario which might be unlikely.

The included table and graph give a summary of the estimated expenditures per policy area. The amounts are the sum of the investments (on time off costs) and the regular (yearly) costs. As shown in the table, some of the policy areas require a marginal expenditure.

More information on the budgetary aspects is included in annex 8.

Area	Amount in 1.000€	%
Area 1. Network of Centres of Expertise	98.914	55,0%
Area 2. Registries	3.250	1,8%
Area 3. Communication	2.550	1,4%
Area 4. Patient empowerment	830	0,5%
Area 5. Education and training caregivers	400	0,2%
Area 6. Improvement of access to diagnosis	5.830	3,2%
Area 7. Improvement of access to medical therapy	23.450	13,0%
Area 8. Comprehensive care	28.800	16,0%
Area 9. Stimulation of research	12.000	6,7%
Area 10. Management of the Plan	3.700	2,1%
Area 11. Ethics and governance	150	0,1%



6. ANNEXES

Annex 1. Lists with Reference Centres and Centres for Human Genetics

Referentiecentra voor zeldzame monogenische erfelijke metabole ziektes / Etablissements de rééducation Maladies métaboliques monogéniques héréditaires rares[83]

Centrum voor Erfelijke Metabole Aandoeningen, Universitair Ziekenhuis Antwerpen, Wilrijkstraat 10, 2650 EDEGEM, Tel. 03/821.38.10 - Kon. Paola Kinderziekenhuis, ZNA Middelheim, Lindedreef 1, 2020 ANTWERPEN.

Unité Métabolique, Hôpital Universitaire des Enfants Reine Fabiola - Metabool centrum AZ-VUB, Avenue J.J. Crocq 15, 1020 BRUXELLES (LAEKEN), Tel. 02/477.25.81, Fax. 02/477.25.63.

Centre des Maladies Métaboliques Héréditaires, Cliniques Universitaires Saint-Luc, Avenue Hippocrate 10, 1200 BRUXELLES (WOLUWE-SAINT-LAMBERT), Tel. 02/764.11.11, Fax. 02/764.37.03.

Centre de Génétique Humaine, Institut de Pathologie et de Génétique, Avenue Georges Lemaitre 25, 6041 GOSSELIES, Tel. 071/44.71.57, Fax. 071/44.71.56.

Centre Pinocchio, Clinique de L'Espérance, Rue Saint Nicolas 447, 4420 MONTEGNEE, Tel. 04/224.80.01, Fax. 04/224.86.09.

C.U.W.G. Maladies Métaboliques, Centre hospitalier universitaire de Liège, Dom. Univ. du Sart-Tilman B-35, 4000 LIEGE, Tel. 04/366.71.24, Fax. 04/366.81.46.

Kliniek voor Kinderziekten "C. Hooft", Universitair Ziekenhuis, De Pintelaan 185, 9000 GENT, Tel. 09/240.35.78, Fax. 09/240.38.75.

Centrum voor Metabole Ziekten, Universitaire Ziekenhuizen Leuven, Herestraat 49, 3000 LEUVEN, Tel. 016/34.38.41, Fax. 016/34.38.42.

Referentiecentra voor mucoviscidose / Centres de référence Mucoviscidose[84]

Associatie Mucoviscidosecentrum Antwerpen, Universitair Ziekenhuis Antwerpen, Wilrijkstraat 10, 2610 EDEGEM.

Universitair Ziekenhuis Brussel, Mucovicidosereferentiecentrum, Laarbeeklaan 101, 1090 BRUXELLES (JETTE), Tel. 02/477.56.00, Fax. 02/477.60.74.

Cliniques Universitaires Saint-Luc, Centre de référence de la mucovicidose UCL, Saint-Luc, Secrétariat de pneumologie-pédiatrique, Avenue Hippocrate 10, 1200 BRUXELLES (WOLUWE-SAINT-LAMBERT), Tel. 02/764.13.82, Fax. 02/764.89.11.

Hôpital Erasme- Hôpital des Enfants Reine Fabiola, Institut de Mucoviscidose ULB, Route de Lennik 808, 1070 BRUXELLES (ANDERLECHT), Tel. 02/555.32.02, Fax. 02/555.34.66.

Centre Liégeois de rééducation fonctionnelle pour la mucovisidose, CHR de la Citadelle, Bd du XIIéme de ligne 1, 4000 LIEGE, Tel. 04/225.70.73.

U.Z. Gent, Referentiecentrum voor Mucoviscidose, De Pintelaan 185, 9000 GENT, Tel. 09/240.39.66.

Muco-Referentiecentrum Gasthuisberg Leuven, UZ Gasthuisberg, Herestraat 49, 3000 LEUVEN, Tel. 016/34.38.95.

83 http://www.riziv.fgov.be/care/all/revalidatie/general-information/contacts/pdf/7890.pdf

84 http://www.riziv.fgov.be/care/all/revalidatie/general-information/contacts/pdf/7891.pdf

Referentiecentra voor neuromusculaire ziektes / Centres de référence Maladies neuromusculaires[85]

U.Z. Antwerpen, Neuromusculair referentiecentrum, Wilrijkstraat 10, 2650 EDEGEM, Tel. 03/821.30.00

Universitair Ziekenhuis Brussel, Neuromusculair referentiecentrum - De Bijtjes, Laarbeeklaan 101, 1090 BRUSSEL (JETTE), Tel. 02/477.50.00, Fax. 02/477.57.83.

Cliniques Universitaires Saint-Luc, Centre de référence neuromusculaire UCL, Saint-Luc, Anvenue Hippocrate 10, 1200 BRUXELLES (WOLUWE-SAINT-LAMBERT), Tel. 02/764.13.11, Fax. 02/764.90.52.

CHR de la Citadelle, Centre Liégeois pour les Maladies Neuromusculaires, Services de Neuropédiatrie et Neurologie, Boulevard du 12e de Ligne 1, 4000 LIEGE, Tel. 04/225.69.81, Fax. 04/225.75.50.

U.Z. Gent, Referentiecentrum voor musculaire aandoeningen, De Pintelaan 185, 9000 GENT, Tel. 09/240.35.93, Fax. 09/240.38.75.

U.Z. Leuven, UZ Gasthuisberg, Neuromusculair referentiecentrum, Herestraat 49, 3000 LEUVEN, Tel. 016/34.42.80, Fax. 016/34.42.85.

Centra voor menselijke erfelijkheid[86] / Centres de génétique humaine

Centrum Medische Genetica, Universiteit Antwerpen, Universiteitsplein 1, 2610 WILRIJK, Tel. 03/820.25.70.

Dienst Medische Genetica, Academisch Ziekenhuis VUB, Laarbeeklaan 101, 1090 BRUSSEL, Tel. 02/477.60.71.

Centrum voor Medische Genetica, Universitair Ziekenhuis Gent, De Pintelaan 185, 9000 GENT, Tel. 09/240.36.03.

Centrum voor Menselijke Erfelijkheid, Universitair Ziekenhuis Gasthuisberg, Herestraat 49, 3000 LEUVEN, Tel. 016/34.59.03.

Centre de Génétique Humaine de l'IPG, Avenue Georges Lemaître, 25, 6041 GOSSELIES, Tel. 071/47.30.47, Fax. 071/47.15.20.

Centre de génétique médicale de l'UCL, Av. Hippocrate, 10, 1200 BRUXELLES, Tel. 02/764.67.74, Fax. 02/764.69.36.

Service de génétique médicale de l'ULB, Hôpital Universitaire Erasme, Route de Lennik, 808, 1070 BRUXELLES, Tel. 02/555.64.30, Fax. 02/555.64.40.

Centre de Génétique Humaine de Liège, Centre Hospitalier Universitaire du Sart Tilman Bloc central Bât B35 4000 LIEGE, Tel.04/366.81.45, Fax. 04/366.81.46.

85 http://www.riziv.fgov.be/care/all/revalidatie/general-information/contacts/pdf/7892.pdf

86 http://www.zorg-en-gezondheid.be/Zorgaanbod/Preventieve-gezondheidszorg/Centra-voor-menselijke-erfelijkheid/

Annex 2. Criteria for Centres of Expertise

E criteria are essential/obligatory.
O criteria are optional/informative.
D criteria: obligation to develop within a specific timeframe (3 or 5 years).

Certification	
E1	**National/international networking with other centres of expertise (funded or not)**
D2	Accreditation of the centre (e.g. accreditation of stem cell therapy unit [JACIE]; accreditation of laboratory facilities [BELAC])
D3	Accreditation of the hospital (e.g. ANAES [FR], NIAZ [NL], JCAH [US])
Basic / Translational / Clinical research	
E4	**Basic / translational / clinical research concerning a specific (group of) rare disease(s) (Last three years are taken into consideration)**
E5	**Number of published studies?**
O6	Basic/translational/clinical?; Phase one/phase two/phase three?
O7	Investigator-driven/Pharma-driven/Organisation-driven (= paid for by an [international] organisation)?
O8	For clinical studies: National/international?; Monocentre/multicentre?; Primary/secondary investigator?
Multidisciplinarity	
E9	**Multidisciplinary consultations**
E10	**Follow existing guidelines for rare disease (e.g. clinical pathways) (formalised – on paper – and effectively used). Participate in development of new guidelines.**
O11	Joint staff meetings
Number of patients	
E12	**Number of new cases of hospitalised and ambulant patients treated by the expertise centre (a patient can only be included if he had at least one hospitalisation or one consultation during the past year / last three years)**
O13	Source: e.g. rapport annuel de l'hôpital/Jaarverslag van het ziekenhuis; MKG/RCM
O14	Figures for the past year (and for the last three years)
Number of staff	
E15	**# permanent FTE medical staff dedicated to the (group of) rare disease(s) Average over the last three years**
O16	# FTE paramedical staff dedicated to the (group of) rare disease(s)

Outcome measurement	
D17	**Outcome measurement at the level of the centre of expertise (yes/no?; type?) (e.g. mortality rate; event-free survival; Quality of Life [QoL] measurement [can replace 'tevredenheidsenquête' / 'enquête de satisfaction'])**
Patient services	
E18	**Structured contact with patient advocacy organisations dedicated to the specific rare disease / group of rare diseases**
E19	**Structured patient information (e.g. patient brochures; dedicated internet sites, informational conferences)**
E20	**Open up an information channel to patients and the general public (e.g. centralised telephone number for questions, Q&A response on website)**
O21	Languages
O22	Help for family members (e.g. staying the night; psychological support)
O23	Reception
O24	Room
O25	Food
O26	Complaints (# of complaints registered; handling)
O27	Patient wellness initiatives
Scientific activity	
E28	**Citation score of the permanent team pertaining to the expertise**
E29	**Active involvement in Biobanking**
O30	Publications: basic/translational/clinical research
O31	Research funding FWO/IWT/other
Teaching activity	
E32	**# of trainees (PhD, postgrad, GSO) for the (group of) rare disease(s)**
E33	**# of specific conferences for the (group of) rare disease(s)**
O34	Organisation of conferences (by RDC/national/international) Active participation (poster/speech) (national/international)
E35	**Membership international scientific associations (~ networking)**

Technical environment	
E36	**Specific diagnostic test(s) for the rare disease** **Special techniques / equipment (imaging, transplantation, gene therapy, etc.) for the diagnosis / treatment of the rare disease**
O37	Development of new techniques or tests
D38	**ICT environment / use of e-health**
Turnaround time	
O39	Waiting time in order to get an appointment (= waiting list)
O40	Time lapse between sample taking and diagnosis Caveat: a minimum time lapse is needed to ensure sufficient quality Other regulations exist for this.
O41	Time lapse between diagnosis and treatment
O42	Number of undiagnosed patients
Other criteria	
E43	**Set up networks with peripheral hospitals, specialists, GPs, paramedical and other care providers for day-to-day care of the patient**
O44	Short-track system in case of emergency
O45	Attractiveness indices — distance between patient and hospital (e.g. postal codes of patients —> MKG/RCM) — (# of second opinions)

Annex 3. Criteria for Liaison centres for Rare Diseases

E criteria are essential/obligatory.
O criteria are optional/informative.
D criteria: obligation to develop within a specific timeframe (3 or 5 years).

Certification	
E1	**Located within a University Hospital in partnership with Centre for Human Genetics and recognised Centres of Expertise (at least 3).**
E2	**National/international networking with other Liaison Offices.**
D3	Accreditation of the hospital (e.g. ANAES [FR], NIAZ [NL], JCAH [US])
Basic / Translational / Clinical research	
E4	**Research concerning rare diseases that are not rare cancers (Last three years are taken into consideration)**
E5	**Number of studies? Minimum of 3**
O6	Number of rare disease patients included in the clinical studies? (ratio: # rare disease patients included in the studies/total # rare disease patients treated in the RDC)
O7	Basic/translational/clinical?; Phase I/II/III?
O8	Investigator-driven/Pharma-driven/Organisation-driven (= paid for by an [international] organisation)?
O9	National/international?; Monocentre/multicentre?; Primary/secondary investigator?
Multidisciplinarity	
D10	**General multidisciplinary consultations** **(This will become an essential criterion after the first evaluation by the Platform)**
E11	**Guidelines for rare diseases (e.g. clinical pathways) (formalised – on paper – and effectively used)** **Minimum 1/3 of the expertises present in the Liaison Office?**
E12	**Joint staff meetings**
O13	Frequency of joint staff meetings?
Number of patients	
E14	**Total number of hospitalised rare disease patients treated by the Liaison Office (at least one hospitalisation during the past year / last three years)**
E15	**Total number of ambulant rare disease patients treated by the Liaison Office (at least one consultation during the past year / last three years)**
O16	Source: e.g. rapport annuel de l'hôpital/Jaarverslag van het ziekenhuis; MKG/RCM
O17	Figures for the past year (and for the last three years)

Number of staff	
E18	**Total # FTE medical staff dedicated to rare diseases** **Average over the last three years; only permanent staff taken into consideration**
O19	Total # FTE paramedical staff dedicated to rare diseases
Outcome measurement	
E20	Outcome measurement (yes/no?; type?) (e.g. mortality rate; event free survival rate; Quality of Life (QoL) measurement [can replace 'tevredenheidsenquête'/'enquête de satisfaction'])
Patient services	
E21	**Structured contact with patient advocacy organisations**
E22	**Structured patient information (e.g. patient brochures; dedicated websites)**
E23	**Open up an information channel to patients and the general public (e.g. centralised telephone number for questions, Q&A response on website)**
O24	Languages
O25	Help for family members (e.g. staying the night; psychological support)
O26	Reception
O27	Room
O28	Food
O29	Complaints (# of complaints registered; handling)
O30	Patient wellness initiatives
Scientific activity	
E31	**Total citation score of the team dedicated to rare diseases (only staff with at least 20% dedication to rare diseases).** **Minimum to be defined**
O32	(Publications: basic/translational/clinical research)
O33	(Research funding FWO/IWT/other)

Teaching activity	
E34	**# of trainees (PhD, postgrad, GSO)** **Minimum to be defined**
O35	# PhD students # Postgraduate students (fellows) # Médecin candidat spécialiste en formation/Geneesheer specialist in opleiding (GSO) # paramedical students
E36	**# of conferences** **Minimum to be defined**
O37	Organisation by the RDC or national/international conferences? Active involvement (poster/speech) in national/international conferences
E38	**Membership international scientific associations (~ networking)**
O39	Passive or active participation (officers)?
Technical environment	
E40	**Special techniques/equipment (imaging, transplantation, gene therapy, etc.)** **Number of patients treated or diagnosed with these special techniques/equipment**
O41	Development of new techniques
E42	**ICT environment/use of e-health** **Procedure to be developed**
Turnaround time	
O43	Waiting time in order to get an appointment (= waiting list)
O44	Time lapse between sample taking and diagnosis Caveat: a minimum time lapse is needed to ensure sufficient quality Other regulations exist for this.
O45	Time lapse between diagnosis and treatment
O46	Number of undiagnosed patients
Other criteria	
E47	**Set up networks with peripheral hospitals, specialists, GPs, paramedical and other care providers for day-to-day care of the patient**
O47	Short-track system in case of emergency
O48	Attractiveness indices — distance between patient and hospital (e.g. postal codes of patients —> MKG/RCM) — (# of second opinions)

Annex 4. Explanation of some concepts on orphan drugs used in area 7

Clinical trial

A clinical trial is a research study to answer specific questions about vaccines or new therapies or new ways of using known treatments. Clinical trials (also called medical research and research studies) are used to determine whether new drugs or treatments are both safe and effective. Carefully conducted clinical trials are the fastest and safest way to find treatments that work in people. Trials are in four phases: Phase I tests a new drug or treatment in a small group; Phase II expands the study to a larger group of people; Phase III expands the study to an even larger group of people; and Phase IV takes place after the drug or treatment has been licensed and marketed.
(*http://www.clinicaltrial.gov/ct2/info/glossary*)

Compassionate Use Programme (CUP)

All medicinal products must be authorised before they can be marketed in the European Union. However, a treatment option for patients in the European Union suffering from a disease for which no satisfactory authorised alternative therapy exists or who cannot enter a clinical trial, may be the use of an unauthorised medicinal product in a compassionate use programme. Compassionate use programmes are intended to facilitate the availability to patients of new treatment options under development. National compassionate use programmes, making medicinal products available either on a named patient basis or to cohorts of patients, are governed by individual Member States legislation.
(*http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000293.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058007e691*)

Medical Need Program (MNP)

By the law of 1 May 2006 on the revision of the pharmaceutical legislation, Belgian has not only adapted the 'Compassionate Use Programs' according to EU legislation, but has also recognised 'Medical Need Programs'. The essential difference between both programs is that Compassionate Use Programs apply to drugs that do not yet have a market authorisation while Medical Need Programs already have a market authoriastion for a specific indication.
(*http://www.fagg-afmps.be/nl/binaries/methode-werk-CU-MNP_tcm290-27169.pdf*)

Orphan drug designation

To qualify for orphan designation, a medicine must, according to the European Medicines Agency (EMA), meet one of these criteria:

- It is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than 5 in 10,000 people in the EU at the time of submission of the designation application;
- It is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and without incentives it is unlikely that the revenue after marketing of the medicinal product would cover the investment in its development.

In both cases, there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorised in the Community or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition.
Sponsors of medicines that have received orphan designation from the European Commission benefit from a number of incentives. These aim to stimulate the development of medicines to treat rare diseases.
(*http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000029.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800240ce*)

Marketing authorisation
The approval granted by the appropriate Regulatory Authority to market a specific medicinal product in a particular country. Under the so called 'centralised procedure', companies submit a single marketing-authorisation application to the European Medicines Agency. Once granted by the European Commission, a centralised (or 'Community') marketing authorisation is valid in all European Union (EU) and EEA-EFTA states (Iceland, Liechtenstein and Norway).
(*http://www.ema.europa.eu/docs/en_GB/document_library/Other/2010/12/WC500099907.pdf*)

Drug reimbursement
In Belgium patients often do not pay the full price for a drug or a medical act. The Belgian social and health care security system pays this expense in part or in full (in the case of orphan drugs). But all health care systems need to make choices regarding services and products that can be covered out of public resources, i.e. they have to set reimbursement priorities, taking all health system objectives into account. Policy measures, such as drug reimbursement systems, are developed to find a publicly acceptable balance between these objectives.
(*http://www.kce.fgov.be/index_en.aspx?SGREF=9470&CREF=18732*)

Off-label use of medicinal products
Off-label use is the term used for the treatment of patients with a drug for and indication or under conditions that are not mentioned in the conditions of the marketing authorisation, and therefore are not on the 'product label'. Off-label can mean use for a different indication, but also a different age category (typically children) or even dosage.

Annex 5. List of materials for compounding used to treat rare diseases[87] (created by members of the Fund for Rare Diseases and Orphan Drugs)

3,4-Diaminopyridine
d,l-3-Hydroxybutyrate sodium
Amiloride
beta-Carotene
Bi-Myconase
Chenodesoxycholic acid
l-Citrulline
CoEnzyme Q10
Diphencyprone
d-Mannose
d-Ribose
Fenfluramine
Glycine
Hydroxocobalamine
Oxybutinine
Phenylbutyrate sodium
Primaquine phosphate
Pyridoxal phosphate
Squaric acid dibutyl ester

87 *List of materials not mentioned in the 'Lijst vergunde grondstoffen/Liste des matières authorisées' (Belgisch Staatsblad/Le Moniteur belge, 396, 10 nov 2004).*

Annex 6. Comprehensive patient care

Introduction

In the healthcare system, each group of persons suffering from a rare disease can be compared to a single individual, lost in the crowd.[88]
Care for patients suffering from a rare disease is not guaranteed and remains uncertain[89]. This is true from the medical point of view in the strict sense, the material point of view and in terms of assistance suited to the special needs resulting from a given specific disease.

The 'Non-RIZIV/INAMI Costs' working group could not limit its considerations to the specific benefits that might be applicable only for a given disease in virtue of the fact that the characteristics of the disease in question were rare. 'Non-RIZIV/INAMI' does not simply mean excluded from RIZIV/INAMI reimbursement, but also and most importantly that the RIZIV/INAMI system in its present form has some shortcomings in addressing this problem. If a patient has a rare disease this does not necessarily mean that the symptoms, treatments, materials required and social consequences are 'original'. However, these symptoms, treatments, shortcomings and needs stand out because of their acuteness, intensity, duration, the difficulty managing them in daily life, and their impact on the quality of life and life expectancy. It is useful to point out in this respect the characteristics of the population affected by the diseases concerned, characteristics listed in the French National Plan for Rare Diseases 2005-2008.[90]

> Onset at an early age: before the age of two in two cases out of three
> The onset of a motor, sensorial or intellectual deficit in one of every two cases, which leads to incapacity reducing autonomy in one of every three cases
> A life-threatening situation in almost half the cases, with rare diseases representing 35% of deaths before the age of one, 10% between the ages of one and five, and 12% between the ages of five and 15.

We referred to the concept of 'differentiated needs-based organisation'. This means in practice that:

> For most users who can live independently there will be a low level of inclusion. Assistance and information will be basic, provided essentially on request.
> For a number of users, there will be a mid-level system of inclusion, with information and services more readily available ('We are there when you need us').
> For a few users, support must be intense and services will be tailored to their needs.

It is at the latter level of needs that most patients with a serious rare disease are, at least if you look at 'the common characteristics of rare diseases' given by Eurordis in November 2005.[91]

88 *Mucoviscidosis, for example, is generally said to be 'the most frequently occurring serious genetic disease in Belgium'. However, it affects (we dare not say 'it affects only') 1,200 Belgians.*

89 *Certain rare diseases with known frequency are registered to a far more limited extent than might be expected. Specialists estimate the number of patients suffering from ciliary dyskinesia in Belgium at between 100 and 200 whereas the frequency is between 1/15,000 and 1/30,000. It can be concluded that 200 to 400 patients suffering from this rare and serious disease are not diagnosed and suffer from 'recurrent infections' or 'unexplained dizziness', etc.*

90 *http://www.orpha.net/actor/Orphanews/2006/doc/plan_national.pdf p.5*

91 *http://www.eurordis.org/IMG/pdf/princeps_document-EN.pdf p.5*
'Rare diseases are severe to very severe, chronic, often degenerative and life-threatening; the onset of the disease occurs in childhood for 50% of rare diseases; Disabling: the quality of life of rare diseases patients is often compromised by the lack or loss of autonomy; Highly painful in terms of psychosocial burden: the suffering of rare disease patients and their families is aggravated by psychological despair, the lack of therapeutic hope, and the absence of practical support for everyday life; Incurable diseases, mostly without effective treatment. In some cases, symptoms can be treated to improve quality of life and life expectancy; Rare diseases are very difficult to manage: families encounter enormous difficulties in finding adequate treatment'

We propose a diagram of the care process for patients suffering from a rare and serious disease. This diagram is a work in progress to which input may be added bit by bit. It allows for:

> Gradual entry into the model, disease by disease, or group of diseases by group of diseases
> Gradual inclusion of new approaches, new discoveries, new responses to needs
> The experimental field represented by each rare disease entering the model can lead to the development of recommendations (guidelines) useful for other pathologies
> Identification of the bodies that can play a role, make suggestions, implement, assess and control
> Discussion of all useful forms of cooperation and exchange of information. This can include the annual reports of centres (centres of expertise (CE), liaison centres, genetics centres), RIZIV/INAMI, the Observatory for Chronic Diseases, the proposed Platform for Rare Diseases, etc.

The model under consideration is designed exclusively for rare and serious diseases. Certain rare diseases have sub-types of varying levels of severity. However, the less serious and simpler sub-types may require care and other intense needs during more limited periods. We propose not to exclude any sub-type of these rare diseases of complex form from the Recommendations and proposals for the Belgian Plan for Rare Diseases.
The model certainly implies considerable commitments and policies, but these are conceivable precisely because they target only a limited group whose needs are greatest.
It is because the diseases are rare that the law has failed to take into account all the special aspects of this category of users. This is perfectly understandable: the law establishes a general framework, then accounts for smaller categories and proposes responses for them. So it is not a question of favouring certain persons compared with the population at large, on the pretext that they suffer from a disease that occurs rarely, but simply of placing them on the same level as others in terms of responding to their needs. The idea is to implement measures suited to the specific needs of patients and thus place everyone on the same level, without positive or negative discrimination. The recommendations aim to develop measures that meet neglected or partially covered needs.

Guidelines for comprehensive patient care
(see also the diagram at the end of this Annex)

Emphasis is placed on Centres, whether Centres of Expertise (CE), Liaison Centres, Genetics Centres or consultants (external experts in a given disease who will be placed on a list and can be consulted).
Such Centres are given responsibilities in the medical management of persons suffering from a serious or potentially serious rare disease and in securing the rights of such persons, to be exercised in terms of their needs.
The diagram implies the drafting of lists of needs related to a given disease and of rights that may be exercised in terms of these needs, based on established criteria.

The recommendations will be grouped and will lead to MEASURES. These measures will concern the patient's care process, needs and rights, monitoring, evaluation, etc.

Recommendation 1: The key role of the Centre
All patients suffering from a rare and serious disease (according to the definition given in the introduction) are referred to a Centre even if immediate medical attention is not required. For certain diseases or groups of diseases, the Centre limits its action to proposing simplified medical care as well as paramedical and social assistance.

Advantages:

> Registration of all patients concerned
> Earlier diagnosis
> Access to information about the disease, its evolution, transmission, treatments, other needs, social consequences, etc.
> Access to the network set up by the centre and to other networks (patient organisations, local networks, etc.)

Recommendation 2: Exchanges with foreign Centres
If expert advice is lacking in Belgium, the Centre refers to experts in other countries. The additional costs involved in such an initiative are paid by insurance carriers.
The two-way system also works in the opposite direction and Belgian Centres will aim to become recognised European Centres of Expertise to which foreign Centres can refer their patients.

Recommendation 3: The patient's comprehensive needs: role of the Centre at the start of the care process
The Centre carries out a complete assessment of the patient

> The category diagnosis and stage of the disease
> The functional diagnosis (ICF International Classification of Functioning)

The Centre presents a proposal for treatment based on this assessment.

Recommendation 4: Lists of needs

Lists of needs related to each rare and serious disease (or group of diseases) will be drafted.
These lists are a work in progress.

Procedure:

> Input is provided to the lists through permanent attention to patients (and patient organisations), service providers and insurance carriers. The future Observatory of Chronic Diseases will be a partner of choice for the exchange of ideas.
> Lists will be drawn up through cooperation between Centres.
> The competent bodies, including the Scientific Council, will give their approval.
> The final decision will be taken by RIZIV/INAMI or by the competent body/bodies.

Recommendation 5: Grant of rights

The decision to grant rights in response to the needs placed on this list is the competence of:

> RIZIV/INAMI, which will give its agreement in the light of existing criteria or will create very specific rights for these target groups
> Other federal or regional bodies, which will also determine an adaptation of their regulations in terms of the specific needs of a given rare and serious disease.
> This implies cooperation and coordination between the different bodies (cf. Competent Bodies working group).

Recommendation 6: Competent Bodies working group

Creation of a working group (WG) that brings together all the competent bodies.
The proposed rare disease platform is a privileged partner for proposing subjects to be addressed by this WG and making suggestions for amendments to laws.
Depending on the results of evaluations, decision-makers may also refer to this WG to discuss issues such as the adjustment of rights or a new distribution of tasks.

Recommendation 7: Electronic transmission

The transmission of necessary data to the bodies that grant concrete rights is facilitated by the development of an EDR (Electronic Disability Record): e-health will accommodate this application.

Recommendation 8: Registration of the patient

The Centre transmits (notification) its diagnosis (category and functional) and its suggested treatment plan to the insurance carrier's medical officer.

The medical officer:

> 'flags' ('recognises') the patient
> determines the starting date and the period
> grants entitlement to a set of rights (which, however, can only be exercised on the basis of established criteria)
> communicates the above to the patient and the centre

Recommendation 9: Care in practical terms

The Centre will only activate the rights justified by the patient's needs at that time (stage of the patient's impairment, compliance with Chapter IV criteria, etc.).
For a service provider who provides treatment for the patient but is not associated with the Centre, conventional application procedures are implemented. This is done separately for each right.

The Centre shall take great care to work systematically and closely with the patient's network (primary care physician, physical therapist, nurse, referring specialist, etc.) and to encourage shared care.

Recommendation 10: Monitoring of expenditure at individual level and by Centre

The insurance carrier carries out ex post controls (for example: compliance with Chapter IV criteria, if applicable; compliance with the specific criteria contained in the list for the disease in question).

Recommendation 11: Monitoring of total expenditure

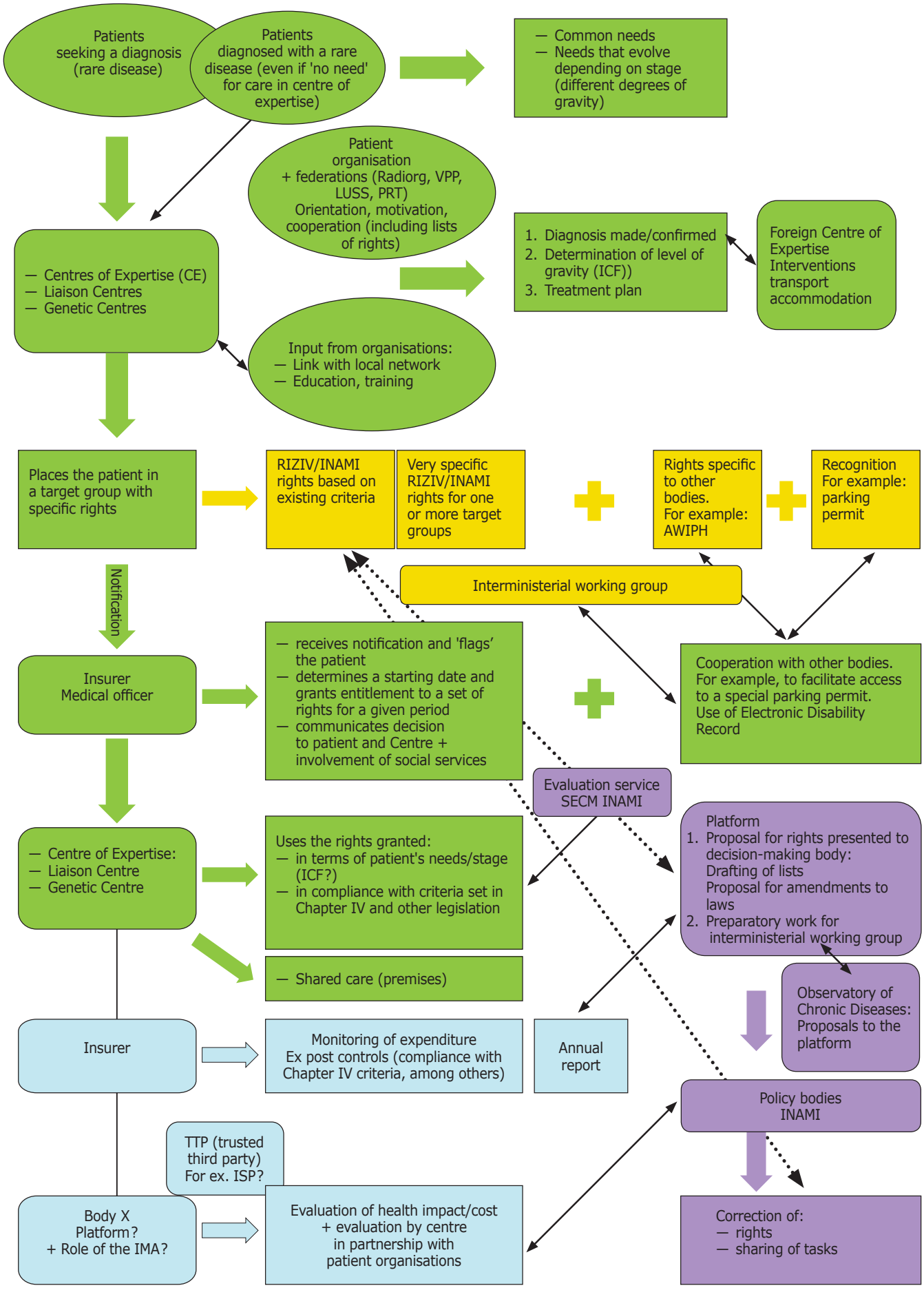
RIZIV/INAMI and IMA (Agence Intermutualiste - Sickness funds agency) monitor expenditure (total, by pathology and by Centre).

Recommendation 12: Evaluation of the system (health impact/cost)

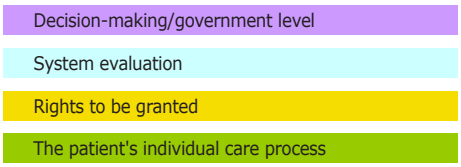
The data provided by the Centres, registries, insurance carriers, IMA, patient organisations, umbrella organisations, the Observatory and the proposed Platform for Rare Diseases are transmitted to a trusted third party (TTP), for example, the Institut de Santé Publique (ISP – Public Health Institute) for comprehensive analysis.

The TTP will analyse the following, among other factors:

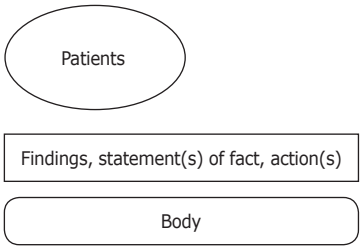
> the health/cost ratio
> evaluation of the functioning of the centres
> networking


Patients seeking a diagnosis (rare disease)
Patients diagnosed with a rare disease (even if 'no need' for care in centre of expertise)
— Common needs
— Needs that evolve depending on stage (different degrees of gravity)
Patient organisation + federations (Radiorg, VPP, LUSS, PRT) Orientation, motivation, cooperation (including lists of rights)
— Centres of Expertise (CE)
— Liaison Centres
— Genetic Centres
1. Diagnosis made/confirmed
2. Determination of level of gravity (ICF))
3. Treatment plan
Foreign Centre of Expertise Interventions transport accommodation
Input from organisations:
— Link with local network
— Education, training
Places the patient in a target group with specific rights
RIZIV/INAMI rights based on existing criteria
Very specific RIZIV/INAMI rights for one or more target groups
Rights specific to other bodies. For example: AWIPH
Recognition For example: parking permit
Notification
Interministerial working group
Insurer Medical officer
— receives notification and 'flags' the patient
— determines a starting date and grants entitlement to a set of rights for a given period
— communicates decision to patient and Centre + involvement of social services
Cooperation with other bodies. For example, to facilitate access to a special parking permit. Use of Electronic Disability Record
Evaluation service SECM INAMI
— Centre of Expertise:
— Liaison Centre
— Genetic Centre
Uses the rights granted:
— in terms of patient's needs/stage (ICF?)
— in compliance with criteria set in Chapter IV and other legislation
Platform
1. Proposal for rights presented to decision-making body: Drafting of lists Proposal for amendments to laws
2. Preparatory work for interministerial working group
— Shared care (premises)
Observatory of Chronic Diseases: Proposals to the platform
Insurer
Monitoring of expenditure Ex post controls (compliance with Chapter IV criteria, among others)
Annual report
Policy bodies INAMI
TTP (trusted third party) For ex. ISP?
Body X Platform? + Role of the IMA?
Evaluation of health impact/cost + evaluation by centre in partnership with patient organisations
Correction of:
— rights
— sharing of tasks

Colour key



Shape key



Annex 7. Evaluation – Comparison with EUROPLAN and indicators

Comparison proposed measures with Europlan indicators			
Areas	**Proposed Measures for a Belgian Plan**	**Europlan indicators**	**Coverage in proposed measures Belgian Plan**
Area 1. Improving the quality of diagnosis, therapy and patient management by setting up expert centres and expert networks	1.1. Creation of Centres of Expertise (CE)	4.1. Existence of a policy for establishing centres of expertise at the national/regional level	part of plan
		4.2. Number of centres of expertise adhering to the policy defined in the country	not defined as number of CE; but defined as number of patients (18000 by year 5)
		4.3. Groups of rare diseases followed up in centres of expertise	not defined in plan; at the moment 3 groups through ref centres; expected to rise significantly
		4.4. Centres of expertise adhering to the standards defined by the Council Recommendations - paragraph d) of preamble	all are expected to as this is part of selection criteria
		4.5. Participation of national or regional centres of expertise into European reference networks	part of plan; means are earmarked
		5.5. Number of diseases included in the neonatal screening programme	Not formally part of Plan. To be discussed with regions and communities
		5.6. Number of diseases included in the neonatal screening programme properly assessed	Not formally part of Plan. To be discussed with regions and communities
	1.2. Strengthen the role of the Centres of Human Genetics (CHG)	5.7. Existence of a public directory/ies of both genetic tests on Rare Diseases	part of plan
		5.8. Proportion laboratories having at least one diagnostic test validated by an external quality control	plan foresees resources to ensure genetic labs obtain quality accreditation
	1.3. Creation of Liaison Network RD		
	1.4. Networking between Centres at national level		
	1.5. Networking between Centres and peripheral care services		
	1.6. Networking at European and international level	Cfr 4.5	

Area 2. Codifying and inventorying rare diseases	2.1. National Belgian Registry for Rare Diseases	2.1. adoption of EC RD definition	part of plan
		2.2. Type of classification used by the health care system	CD 11
		2.3. Developing policies for recognising RD by the care information systems	part of plan
		2.4. Registering activity	part of plan
		2.5. Number of diseases included	resources are defined in plan, but not the number of diseases (max number with resources available)
Area 3. Information and communication	3.1. Creation of a national portal website with actual and validated information		
	3.2. Support for Orphanet Belgium		
	3.3. Communication Plan		
Area 4. Patient empowerment	4.1. Empower patients in their relation to health care professionals	6.1. Number of umbrella organisations specific on RD	one existing (RaDiOrg.be,the Belgian Eurordis representative); involved in plan
	4.2. Enforceable patient participation at the start up, functioning and evaluation of Centres of Expertise	6.2. Having a directory of RD patients organizations	responsibility of Radiorg.be
	4.3. Improvement of the collaboration between patient organisations	6.3. Number of Patients' associations	rare disease associations estimated at 150, Monitoring is part of Orphanet remit (part of plan)
	4.4. The development of a medical passport	6.4. Number of diseases covered by patients' associates	not known; every CE will be linked with disease specific association(s)see also Orphanet
		6.5. Permanent and official patients' representatives in plan development, monitoring and assessment	part of plan
		6.6. Participation of patients organizations in the development of RD research strategies	part of plan
		6.7. Participation of patients organizations in the RD centres of expertise designation and evaluation	part of plan
		6.8. Resource (funding) provided for supporting the activities performed by patient organisations	part of plan (120 K € first year, growing to 200 K € in 5th year)

Comparison proposed measures with Europlan indicators			
Areas	**Proposed Measures for a Belgian Plan**	**Europlan indicators**	**Coverage in proposed measures Belgian Plan**
		6.9. Support to sustainable activities to empower patients, such as awareness raising, capacity-building and training, exchange of information and best practices, networking, outreach to very isolated patients	part of plan
		6.10. Avalability of Help line for RD	part of plan
Area 5. Training and education of health professionals	5.1. To integrate education and teaching about rare diseases (and orphan drugs)	5.1. Existence of a comprehensive national and/or regional RD information system supported by the government	part of plan
	5.2. Creation of a specific and additional category on continous medical education (CME) accreditation in rare diseases by RIZIV/INAMI	5.2. Help lines for professionals	Partially covered through Orphanet and measure 4.4 of the Plan
		5.3. Clinical guidelines	part of plan (different measures of area 7)
		5.4. Number of such as activities promoted by the plan/strategy	no number defined, only resources
Area 6. Improving access to and financing of diagnosis	6.1. Change the system to allow DNA-samples to be tested abroad		
	6.2. Access and reimbursement of non-DNA testing and development of such technologies in Belgium		
Area 7. Improving access to and financing of treatment	7.1. Launch an information service on clinical trials, compassionate use and medical need programmes	5.9. Number ODD market authorizations by EMEA and placed in the market in the country	out of 63 Marketing Authorised drugs (EMA); 45 are reimbursed in Belgium. (6 are in procedure, 8 were not yet submitted, 4 refused).
	7.2. Adapt existing legislation to increase transparency and availability of information from compassionate use and medical need programmes	5.10. Time between the date of a ODD market authorization by EMEA and its actual date of placement in the market for the country	estimated at 18 to 24 months; should decrease because of measure proposed for early access
	7.3. Awaiting an adaptation of the EU clinical trials Directive, Belgium should proactively apply the so-called "Voluntary Harmonised Procedure" whenever a request to launch a clinical trial in Belgium for an orphan drug	5.11. Time from the placement in the market in he country to the positive decision for reimbursement by public funds	both decisions are linked

	7.4. Improvements are possible to the way ethics committees are coming to a single opinion in the case of rare diseases where by definition no alternative treatments are available to the patients	5.12. Number of ODD reimbursed 100%	all as of today
	7.5. Academic (non commercial) clinical trials for rare diseases should be stimulated financially and made more visible	5.13. Existence of a governmental program for compassionate use for Rare Diseases	part of plan
	7.6. The role of the Special Solidarity Fund should be clarified		
	7.7. Ensure that materials for compounding used to treat rare diseases, can be used legally		
	7.8. Setting up a system for early access to orphan drugs including early temporary reimbursement		
	7.9. Colleges for orphan drugs have proven to be a good practice. Their role and use could be enhanced and strengthened for a higher impact.		
	7.10. Responsible off-label use of drugs should be possible to treat patients with rare diseases under specific conditions.		
	7.11. Support home treatment for orphan drugs under clear conditions		
	7.12. Stimulate patient adherence through a set of initiatives		
	7.13. Belgium to take a leading role in a number of European issues related to access to treatment for patients with a rare disease		
Area 8. Comprehensive care of the patient	8.1. To simplify the access to measures concerning diagnosis and coordinated treatments, to propose the assistance of a "rare disease care coordinator"	6.11. Existence of official programs supporting patients and families with disabilities	already case
	8.2. To facilitate the access to specialized help, to simplify the administrative procedures	6.12. Existence of an official directory of social resources for patients with disabilities	part of plan

Comparison proposed measures with Europlan indicators			
Areas	**Proposed Measures for a Belgian Plan**	**Europlan indicators**	**Coverage in proposed measures Belgian Plan**
		6.13. Existence of national schemes promoting access of RD patients and their families to Respite Care services	nothing specific foreseen in plan
		6.14. Existence of public schemes supporting Therapeutic Recreational Programmes	nothing specific foreseen in plan
		6.15. Existence of programmes to support integration of RD patients in their daily life	nothing specific foreseen in plan
		6.16. Existence of programmes to support rehabilitation of RD patients	nothing specific foreseen in plan
Area 9. Stimulating research on rare diseases	9.1. Research projects on rare diseases should be made identifiable and traceable within (national) research support programs	3.1. Existing a RD National/Regional research programmes	part of plan
	9.2. Increase national support to E-rare	3.2. RD research programme monitoring	part of plan (through measure 9.1)
	9.3. An impulse program for research on rare diseases	3.3. Number of RD research projects approved by year (if possible yearly starting the year before plan commencement)	part of plan (through measure 9.3)
	9.4. Identification of unmet medical needs	3.4. Clinical trials funded by public bodies	part of plan (through measure 9.3)
		3.5. E-RARE joining	part of plan
		3.6. Including public health and social research, in the field of rare diseases	not foreseen
		3.7. Research platforms and other infrastructures are also funded by the research programme	partially through measure 9.3
		3.8. Number of young scientists recruited every year to work specifically on rare diseases	not recorded
		3.9. There are specific public funds allocated for RD research	part of plan (through measure 9.3)
		3.10. Funds specifically allocated for RD research actions/projects per year since the plan started	part of plan

Area 10. Management of the Plan	10.1. Creation of a National Platform for Rare diseases	1.1. Existence of regulations/ laws that support the creation and development of a RD plan	political decision at national parliament level is the legal base
		1.2. National/regional (percentage of regions)	limited involvement of regions
		1.3. Existence of a coordination mechanism	part of plan
		1.4. Existence of an expert advisory committee	part of plan (platform)
		1.5. Existence of an external evaluation body/procedure	part of plan
		1.6. Number of priority areas included in the plan	10
		1.7. Budget of plan/strategy	160 million over 5 years
		7.1. Existing policy/decision to ensure long-term sustainability of the RD plan/strategy	part of plan
		7.2. Amount of funds allocated for ensuring RD plan/strategy sustainability	87%
		7.3. Existing policy/decision to ensure the contribution to support RD European infrastructures	part of plan
Area 11. Ethics	11.1. Transparency of pricing		
	11.2. Citizens conferences on rare diseases and orphan drugs		

Potential Indicators proposed measures for a Belgian Plan Rare Diseases		
Areas	**Proposed Measures**	**Potential indicators**
Area 1. Improving the quality of diagnosis, therapy and patient management by setting up expert centres and expert networks	1.1. Creation of Centres of Expertise (CE)	Number of centres selected; Number of patients diagnosed/year; Number of patients treated/year; number of diseases covered; Number of reviews and updates of care path; Number of reviews and updates of economic aspects of care paths
	1.2. Strengthen the role of the Centres of Human Genetics (CHG)	Number of labs having accreditation; No of centres having quality management of clinical activity; Average Number of EQA participations/centre; Number of centres member of Eurogentest association; Average Number of person-day participations in quality management related training or events; Existence of a directory of tests offered by centres of CHG publicly available; Number of test types offered on this list;
	1.3. Liaison Network RD	Number of of Multidisciplinary consultations; Number of patients diagnosed;
	1.4. Networking between Centres at national level	Number of networking events/year; satisfaction scores of key stakeholders;
	1.5. Networking between Centres and peripheral care services	Satisfaction score of key stakeholders (care coordinators, managers of centres, liaison officers, patients,…); Number of diseases included in neanatal screening programmes at regional level; Percentage of patients treated (partially) at local level;
	1.6. Networking at European and international level	Number of centres of expertise from other EU countries selected by the Belgian authorities; Number of patients sent abroad for diagnosis; Number of patients (partially) treated with assistance from a CE in another country; Number of EU networking events hosted in Belgium; Number of Belgian CE experts staff participating in EU events/year; Number of Belgian CE that receive a reference centre status at EU level;
Area 2. Codifying and inventorying rare diseases	2.1. National Belgian Registry for Rare Diseases - development costs (generic and disease specific)	Number of patients in registry; Number of disease registries created and integrated; Effective integration of genetic and rare disease registries; degree of europeanisation and internationalisation of registries;
	2.2. Belgian Registry for Rare Diseases - running costs	Satisfaction scores of key stakeholders (patient organisations, industry, scientific community, managers of CE,…)
Area 3. Information and communication	3.1. Creation of a national portal website with actual and validated information	Number of unique visitors by target group; degree of satisfaction of users
	3.2. Support for Orphanet Belgium	Number of unique visitors by target group; degree of satisfaction of users
	3.3. Communication Plan	Awareness of Plan among key stakeholders; awareness of liaison network among key stakeholders; awareness of CE among key stakeholders
Area 4. Patient empowerment	4.1. Empower patients in their relation to health care professionals	Change in opinion among health professionals; Changes identified by experts like patient organisations
	4.2. Enforceable patient participation at the start up, functioning and evaluation of Centres of Expertise	Number of centres having active patient involvement in management and evaluation; Number of patients involved in management and evaluation of individual centres; Number of formal cooperation agreements and service sharing between CEs and patient organisations;

	4.3. Improvement of the collaboration between patient organisations	Number of formal cooperation initiatives; number of members of Radiorg.be
	4.4.medical passport or other instrument for emergency medical information	Number of users
Area 5. Training and education of health professionals	5.1. To integrate education and teaching about rare diseases (and orphan drugs)	Number of course (modules) on RD integrated in formal MD and paramedical curriculum
	5.2. Rare diseases in continous medical education (CME)	Number of courses offered in continuous education
Area 6. Improving access to and financing of diagnosis	6.1. Change the system to allow DNA-samples to be tested abroad	Number of tests performed abroad
	6.2. Access and reimbursement of non-DNA testing and development of such technologies in Belgium	No, of tests performed abroad
Area 7. Improving access to and financing of treatment	7.1. Launch an information service on clinical trials, compassionate use and medical need programmes	Number of unique users/visitors; Number of participants in clinical trials; Number of clinical trials in which Belgian patients participate
	7.2. Adapt existing legislation to increase transparency and availability of information from compassionate use and medical need programmes	Number of participants in clinical trials; Number of clinical trials in which Belgian patients participate
	7.3. Awaiting an adaptation of the EU clinical trials Directive, Belgium should proactively apply the so-called "Voluntary Harmonised Procedure" whenever a request to launch a clinical trial in Belgium for an orphan drug	Number of participants in clinical trials; Number of clinical trials in which Belgian patients participate
	7.4. Improvements are possible to the way ethics committees are coming to a single opinion in the case of rare diseases where by definition no alternative treatments are available to the patients	Number of decisions taken centrally
	7.5. Academic (non commercial) clinical trials for rare diseases should be stimulated financially and made more visible	Funds invested; Inclusion of a specific targeted communication action in the communication plan; Reach among scientists of communication actions as part of communication plan;
	7.6. The role of the Special Solidarity Fund should be clarified	Evaluation of the yearly report of actvities of the SF

Potential Indicators proposed measures for a Belgian Plan Rare Diseases		
Areas	**Proposed Measures**	**Potential indicators**
	7.7. Ensure that materials for compounding used to treat rare diseases, can be used legally	No of materials certified/year
	7.8. Setting up a system for early access to orphan drugs including early temporary reimbursement	Number of requests for early access; average speed of decision/ access for patient
	7.9. Colleges for orphan drugs have proven to be a good practice. Their role and use could be enhanced and strengthened for a higher impact.	Evaluation of the yearly report of the colleges
	7.10. Responsible off-label use of drugs should be possible to treat patients with rare diseases under specific conditions.	Evaluation of initiatives taken by INAMI on this issue; Number of requests at the SSF; Number of patients included in the RD registry being treated with an off-label drug; Existence of an initiatives to collaborate at EU level on treatments using off-label drugs;
	7.11. Support home treatment for orphan drugs under clear conditions	Percentage of patients being treated at home
	7.12. Stimulate patient adherence through a set of initiatives	Ideally: survey of a sample of patients at start and at end of Plan; Effective inclusion of communication actions on this issue in the communication plan; Effective record keeping on adherence at the level of hospital pharmacies; Effective feedback on adherence based on record keeping towards patient; Effective inclusion of adherence related aspects in recommendations on packaging of orphan drugs by EMA; Effecive inclusion of adherence related elements in post marketing information (and therefore in RD patient and disease registries);
	7.13. Belgium to take a leading role in a number of European issues related to access to treatment for patients with a rare disease	Number of Belgian initiatives; Effective revision of clinical trials directive;assessment of improvements of revised clinical; trials directive from RD point of view; Effective clarification of orphan designation definition and criteria; Improvement of speed and efficiency of the decision-making process (market authorisation combined with reimbursement decision); Number of orphan drugs whose post-marketing monitring related registries are integrated in a comprehensive EU-wide disease and patient registry (effectively avoiding multiplication of registries);
Area 8. Comprehensive care of the patient	8.1. To simplify the access to measures concerning diagnosis and coordinated treatments, to propose the assistance of a "rare disease care coordinator"	Number of rare disease coordinator (equivalent full time); Number of patients assisted; degree of satisfaction of patients;
	8.2. To facilitate the access to specialized help, to simplify the administrative procedures	Number of simplifications achieved; Number of patients involved

Area 9. Stimulating research on rare diseases	9.1. Research projects on rare diseases should be made identifiable and traceable within (national) research support programs	Number of projects identified
	9.2. Increase national support to E-rare	Funds invested/shifted to E-rare; Number of projects supported at Belgian level;
	9.3. An impulse program for research on rare diseases	Number of projects submitted; Number of projects approved
	9.4. Identification of unmet medical needs	Effective realisation of an EU-level study on unmet medical needs including those of RD patients;
	9.5. Public funds are available for translational research	Number of projects submitted; Number of projects approved
Area 10. Management of the Plan	10.1. Creation of a National Platform for Rare diseases	Number of care pathways defined; Number of selection processes for Expert Centres started; Effective creation of a management organ; Regularity of meetings of advisory /management organ; Number of Working Groups; Number of meetings of Working Groups; Degree of satisfaction of various stakeholders; Effectiveness of decision-making to adapt Plan to experience and circumstances; Realisation of mid-term and final evaluations;
Area 11. Ethics	11.1. Transparency of pricing	Realisation of a EU-level study on price setting and transparency; Impact of decisions taken on price setting;
	11.2. Citizens conferences on rare diseases and orphan drugs	Number of citizens consultations organised (ad hoc and regular); Number of citizens involved; Satisfaction of stakeholders; Evaluation of process (fairness, inclusiveness);

Annex 8. Budget

This document covers the budget impacts of the potential measures proposed to be included in the Belgian Plan Rare Diseases. These financial impacts are not put in relation to the impacts on patients and other stakeholders, which are described in the Plan itself. The objective of this description is to document the estimates mentioned in the Recommendations and proposed measures for a Belgian Plan for Rare Diseases.

The potential budget impacts of the proposed measures can be grouped in different categories:

- Budget impact (costs – savings) for the reimbursed health services (health insurance).
- Investment costs: these are normally one off costs to create the conditions necessary for a measure to be effective. An example is to create a portal web site, there is an initial cost of design and set-up.
- Yearly implementation costs: these are costs that become fixed costs to ensure a measure is operational. This includes typically salary costs of staff.
- Budgets limited in time: this would be the case e.g. for a programme to boost research in rare diseases. Such a programme, would be allocated for a specific period.

In the cost estimates we have followed some principles:

- The economic value is the basis to include or not include a cost. This means that if a 'task' is taken up by a staff member that is recruited for this task, or is taken up by a public institution who will allocate one of its staff members to the task, the budget impact is the same (the value of one person-year).
- Standard costs are used for staff costs and for overheads. These can vary significantly depending on the institution.

The estimates for each measure are documented below. At the end of this document, there is a conclusion on the impact with a forecast over a 5 year period. Figures are based on 2011 prices. No inflation or adjustments are included.

Measure 1.1: Creation of Centres of expertise

Infrastructure, staffing and financing of Centres

In the current RIZIV/INAMI-conventioned reference centres (neuromuscular disorders, metabolic disorders, cystic fibrosis) the principles for financing are:

- medical acts are paid and reimbursed based on the nomenclature and excluded from the convention;
- the convention pays for the additional cost of multi-disciplinarity and the cost of paramedical staff, both from the point of view of total care (diagnostics, treatment and follow-up of treatment) provided in essence at the centre; each convention therefore defines the type of paramedical staff the centres need to have and puts thresholds (e.g. half-time dietician per 50 patients for metabolic diseases);
- the convention pays for individual patients that receive regular treatment a sum (quarterly or annually); this sum is between 1.500 and 2.500 euro/patient/year on average;
- there is a threshold in number of patients (25 or 50), which means that if a centre does not reach the threshold, the convention does not pay for any patient.

The three conventions together account for approximately 3.500 to 4.000 patients, and a cost to the health insurance system of probably 6 to 7 million Euro.

Another model that exists is the MOC or Multi-disciplinary Oncological Consultation. This is reimbursed separately to ensure consensus building among various disciplines before decision-making on an individual patient treatment. A similar approach could be used for the Multidisciplinary Rare Disease Consultation (MRDC). Such an approach would ensure that the additional costs carried by centres due to the multi-disciplinary nature of the rare diseases are covered. It would however not cover the costs of paramedical and non-medical staff.

The convention model seems adequate for the Centres of Expertise even if the principles with regard to recruitment and evaluation of the centres will be different.

A conclusion from the experience with the conventions is also that although the diseases are different, the average additional cost/patient/year lies in a similar bracket (1500 to 2500 euro/year). This gives an indication of the cost to be expected in the future of setting up more Centres of Expertise.

Impacts for the health insurance budget

- This is extremely difficult to estimate due to the diversity of diseases, the fact the system will lead to savings (unnecessary costs of diagnosis and treatment will be saved), but also to additional costs (patients will e.g. live longer). Based on the experience of the reference centres as they exist today:there is a general consensus that savings are probably offset by additional costs linked to the longer life of patients; savings are therefore not estimated;
- the average cost/year/patient for the diseases covered by the present conventions gives a good indication of the additional costs generated by rare disease patients, when treated through centres of expertise;
- the lump sum as used is generally considered as adequate to cover the costs of multi-disciplinarity and the costs of additional personnel.

The impact calculation proposed is therefore based on the number of patients that will be followed by centres rather than by the number of centres that will be selected.
For the proposed estimate of the average, following elements were taken into consideration that influence and differentiate between the present experience with conventions, and the expectation in the future:

- the expected clustering of CE by groups of diseases;
- the concentration of CEs in university hospitals (80% of CEs?);
- the mix between 'national' CEs en EU-level ultra-rare disease CEs based in Belgium;
- the principles of centralisation of expertise combined with decentralisation of care;
- the differences in need for care depending on the disease;
- the link with measure 8.1 on total care management.

As a conclusion one can estimate an average additional cost per patient per year at the low bracket level mentioned above, or 1800 euro/patient/year.

It is not clear how fast the CEs will be selected and become operational.
If the plan works adequately, one can expect up to 15.000 (additional) patients will have been diagnosed within a five-year period and will be treated annually in the network of CEs, leading to an additional yearly cost of up to 27 million euro/year in the year 2016.
As a comparison:

- the centres for Human Genetics are estimated to see in total some 10.000 patients/year for counselling. This number includes new patients, but also patients that were diagnosed in the past. It also includes family members. 80% of rare disease patients are estimated to have a genetic disease;
- the networks of RIZIV/INAMI-conventioned reference centres (neuromuscular disorders, metabolic disorders, cystic fibrosis) are treating 3.500 – 4.000 patients/year.

Defining the cost of rarity and multidisciplinarity

The actual reimbursement level will be defined at the moment a call for expressions of interest is launched for one or more CE for a specific disease. At that moment, experts should have defined the diagnostic and therapeutic pathway for that disease based on the best practice information in Belgium and internationally. This pathway should be translated in economic terms, and in this analysis the difference should be made between the medical acts falling under the nomenclature, and the medical acts that are linked to the rarity of the disease (typically the cost of the multidisciplinarity) and the exceptional characteristics of the therapy (e.g. need to define a diet and follow-up on this diet). This economic analysis should be documented and part of the regulatory basis defining the relationship between the CE and the RIZIV-INAMI. It should be reconsidered each time the therapeutic pathway is changed, and in the absence of a change, on a regular basis (yearly). This regular review should be based on a monitoring of costs in and by each CE (including the use of timesheets) and benchmarking between CEs in Belgium and ideally with CEs for the same disease in other EU countries. This review should be done by a panel of experts and patients.

A specific budget is foreseen to manage this activity at the level of the National Platform and in close cooperation with RIZIV/INAMI.

This budget is estimated to grow to 200.000 euro/year. This includes a management position half time (in charge of managing and facilitating the system of panels), and a support function (for organisational aspects) also half time, and a budget of 100.000 euro to pay the costs generated by the panels, including fees and expenses for panel participants.

Although this cost is linked to this measure, it is included as part of the budget of measure 10 (management of the Plan).

Although this budget appears as a cost, one should consider this approach will help to keep the total cost of running the CEs down. This will be realised by keeping a strong focus on cost issues, on transparency, including through benchmarking and transfer of good practice between CEs, and reactivity to changes.

Reimbursing costs of patients sent to centres of expertise in the EU

As mentioned above, it is expected that Belgian patients will be sent abroad when they have a disease not covered by one of the Belgian centres for rare diseases. Different situations can be expected:

- patients that are sent abroad as part of the process to make the right diagnosis; after diagnosis, they come back and are treated in Belgium;
- patients who are sent abroad to define the right treatment; after the treatment is defined, the patient is followed in Belgium by a CE or a Liaison Office Rare Diseases;
- patients who are sent abroad for a full treatment.

The last category is expected to be very small.

The costs linked to the care of the patients in the first two categories is covered by the budget mentioned above and by the budget under measure 8.1 below (care coordination). What is however not covered are the fees that the foreign centres will charge. This is expected to be covered under the cross border directive, and is at this stage virtually impossible to estimate due to the lack of experience and references.

Measure 1.2: Reinforcing the network of Centres of Human Genetics (CHGs)

Although the CHGs play a strategic role in the network proposed to provide adequate services to patients with rare diseases, their financing is independent of the Belgian Plan.

CHGs are expected to become themselves Centre of Expertise for specific rare diseases. The additional costs this will generate for them, would be covered through measure 1.1 and therefore does not appear under this measure 1.2.

Still, a specific budget is proposed for this measure under the plan to cover (part of) the investment costs CHGs need to develop quality management systems and become certified. Quality management is one of the

necessary investments to ensure the CHGs can take up their role in the network and in an EU context. To make a parallel: Belgian patients and samples are expected to be sent to certified EU centres or labs when sent abroad.
The budget proposed is a fund of 400.000 euro that would be made available to the centres to fund investment costs.
CHGs would need to apply for the funds and justify their demands. The funds could be equally split over all CHGs, like they could be allocated based on needs.

Measure 1.3: Creation of a network of RD diagnostic and treatment units for rare disease patients (Liaison network rare diseases)
To finance this role, a different model is proposed. With two different components, one component is linked to each individual patient; the second is a fixed cost for the duration of the plan.

Component 1
The inspiration comes from the MOC or Multi-disciplinary Oncological Consultation. This is reimbursed separately to ensure consensus building among various disciplines before decision-making on an individual patient treatment.
A similar approach could be used for the Multidisciplinary Rare Disease Consultation (MRDC). Such an approach would ensure that the additional costs carried due to the multi-disciplinary nature of the rare diseases are covered. It would however not cover the costs of paramedical and non-medical staff.

This approach does make sense as:
- the liaison centres will work as a network; networking costs could be covered by another budget (management);
- the liaison centres are (likely) all hosted in university hospitals and would work in close cooperation with the CEs hosted inside these hospitals;
- the need to create a strong link between the liaison offices and the 'total care coordination' function as described in measure 8.1.

As for the CEs, the actual budget impact forecasting is very difficult to make. Two assumptions are made:
- the Multidisciplinary Rare Disease Consultation (MRDC) would be reimbursed at 250 euro (no discussion has taken place yet on the actual content or ways to standardise such MRDC);
- all single entry points together would treat 2.000 patients/year for diagnosis.

On top of this, the liaison offices are expected to coordinate the care of patients that were sent to CEs in other EU countries. This is expected to be a percentage of the patients that are treated in national CEs, e.g. 20% of 15.000 after 5 years of National Plan implementation. The cost of this role is not taken into account as:
- these patients might be followed at different levels, depending of the best solution for that specific patient: e.g. in a national CE who would link up with the foreign CE, by the local specialist or even GP following the individual patient;
- this follow-up does not necessarily require 'multi-disciplinarity'; the cost of uni-disciplinary treatment is normally covered through the nomenclature;
- measure 8.1 also will cover a follow-up of these patients.

The total cost of this component of the measure is therefore estimated at 500.000 euro/year.

Component 2
The second component would be to finance the salary of a liaison officer rare diseases.
The budget impact is estimated at one halftime post at senior medical level for each university hospital.
The total cost is estimated at 500.000 euro/year.

Measure 1.4: Networking between Centres at national level
A budget of 50.000 euro/year is earmarked to finance this activity.
The management is at the level of the National Platform, who can use the funds to pay for e.g. an annual conference, best practice dissemination, thematic networking meetings, meetings by groups of diseases, etc.

Measure 1.5: Networking between CEs and peripheral care
The main cost for this activity is covered through measure 8.1 (global care coordination).
A specific budget is still earmarked under this measure to develop a software and communication tool to improve the efficiency of diagnosis and follow-up of treatment, through better sharing of information between the various persons involved:

- within an institution, among the various disciplines;
- between institutions, and particularly centres of expertise, both inside and outside Belgium;
- between centres and first and second line care, including the patient's GP or local specialist, and the paramedical care providers at the local level.

Examples of such tools do exist. The budget is foreseen to develop and roll out a further development of such a tool that would be adapted to the specific need. This is an investment budget, but it is spread over the full period of the plan. The budget earmarked is 250.000 Euro.

Measure 1.6: Networking between Centres at international level

A budget of 50.000 euro/year is earmarked to finance this activity.
The management is at the level of the National Platform, who can use the funds to pay for e.g. participation of staff of centres in international meetings, co-hosting or co-organisation of EU-level meetings, etc.

Measure 2.1: National patient registry
The IPH-WIV is an organisation that could be responsible for the Registry. This institution has the expertise and has estimated the cost based on two factors: the number of variables and the potential number of patients. Comparing these two factors with the experience of running the registry for cystic fybrosis, gives an investment budget (start-up) of below 25.000 euro and operating budget each year that could be up to 200.000 euro. A budget of 200.000 euro is therefore identified for year 1, which is 2011 as this measure was approved as part of phase 1 of the plan.
This budget does not take into account the cost of data entry that would be decentralised in the CE, CHG and CRD. This activity will need financing either by patient/entry (as used for CF) or as part of the global financing of the CE, CHG and CRDs (examples exist in conventions). Because of the limited number of patients and of variables, this cost is estimated at max 15% of the running cost of the registry.

Running a central registry should also be considered as a tool to serve as a basis to link various existing, or to be created, registries for specific diseases.

Measure 2.2: Disease specific registries

The purpose is to link the general patient rare disease registry with disease specific registries. The cost is difficult to estimate as it is linked to both the number of variables to be included and the number of patients.

The different principles that were taken into account to propose a budget for this measure are the following:

- first of all the importance of the measure. Many other measures are based on the existence of such registry, and the existence will lead to better care, better decisions, and a better use of scarce resources in the longer term (link with many of the measures in area 7, which could lead to significant savings in the longer term);
- the need to cooperate at EU level: it makes little sense for Belgium to develop autonomously disease specific registries. This should be done at EU level. Still, this should not be an alibi to do nothing at Belgian level. The expectation is therefore that during the first years, there will be dominance of national level work, but that this will shift to a more efficient use of resources through more EU-level cooperation;
- the investments made in e-care which are expected to lead to better linkages between data-bases and better availability of data. Again, this is no alibi not to get started, but it is obvious that investments needed to start-up new registries will be significantly reduced in a foreseeable future, through the investments made in e-health;
- the initial budget for setting up and running the overall registry (200 K in the first year), cover essentially the costs of a small team, a team that will participate in the setting up of disease-specific registries as well;
- the link between this registry and the registry Centres for Human genetics has to be set up. The hypothesis is that there would be only one national registry grouping genetics and rare diseases.

The proposal is therefore to earmark two different budget from 2012 onwards:

- a yearly budget to cover the development costs, essentially to integrate existing disease registries or develop new ones; this budget should also cover the development costs linked to the expected integration of the registry into an e-care platform where all data is made available to the various caretakers and stakeholders;
- a yearly budget to cover the running costs of the registries.

Both budgets should be used in the most efficient way, through EU-level cooperation, to increase the number of diseases and patients included in the system.

Budgets cover:

- the costs of staff members of IPH-WIV working full or part-time on the setting-up of registries and on their maintenance;
- the costs of setting up new disease-specific registries, each time based on terms of reference, and a formal approval process through the National Platform;
- the costs linked to setting-up and running a scientific committee.

The table below gives an overview of the evolution of the budgets, in the understanding that there would be a bigger investment early in the plan.

Measures	2011	2012	2013	2014	2015	2016	Total
2.1. National Belgian Registry for Rare Diseases - development costs (generic and disease specific)	200	500	500	300	300	200	2000
2.2. Belgian Registry for Rare Diseases - running costs		200	250	250	250	300	1250

Figures are in 1.000 Euro

Measure 3.1: Portal website

The costs for the portal website (on the basis of two offers) have been estimated at:

- initial website development: between 22.000 and 37.000 euro;
- operational yearly cost (maintenance, debugging, updating and server hosting): between 7.500 and 20.700 euro/year;
- 1 FTE for content management: 70.000 euro/year (0,5 FTE for each community).

The costs included in the budget are therefore:

- an investment cost of 30.000 euro for the initial design and set-up of the portal site;
- an operating expenditure of 100.000 euro/year, which would for 70% cover a salary cost.

This cost was already foreseen in phase 1 and therefore in 2011.

Measure 3.2: Orphanet Belgium

For Orphanet Belgium support:

- 1 FTE for content management (70.000 euro/year (0,5 FTE for each community))

For translation of Orphanet into Dutch, several possibilities exist. Orphanet might receive European funding for translating the website (or parts of it) in Dutch. In that case no specific National Belgian funding is needed. If Orphanet does not receive this funding, different scenarios might apply, dependent on which content will be translated:

- full translation of Orphanet: 150.000 euro + 2.000 euro per consecutive year;
- translation of abstracts (patient relevant information): 70.000 euro + 1.000 euro per consecutive year.

The costs included in the budget are therefore:

- an investment cost of 70.000 euro for the translation of the patient-relevant data of the Orphanet web-site;
- an operating expenditure of 75.000 euro/year, which would cover a salary cost and provide for a budget of 5.000 euro/year for translation and other expenses.

This cost is normally part of a separate budget that was approved as part of the Belgian contribution to the EU-level project Orphanet and its financing. As it is relevant and part of the Plan, it is included.

Measure 3.3: Communication Plan

This measure covers in a flexible way the need to invest heavily in communication. The rarity of the diseases means they are unknown, and one of the main challenges of the Plan will be to make sure all the relevant target groups, from first line medical professionals to patients, will find the way to the network of CEs, to the portal web site and to the patient organisations.

The communication plan will be flexible, and lead to yearly objectives and focus. Its management will be the responsibility of the team supporting the National Platform (see measure 10 and the budget for management of the Plan).
Still, a separate budget is earmarked for the investment-related activities in communication.
This includes:

- a budget for public relations towards the press: this is to cover the fees of specialist support, drafting press releases, maintaining relations with the press, organise press conferences, etc. The yearly budget for this function is set at 60.000 euro;
- a budget for campaigns, including for support to Rare Disease Day. These campaigns can have different themes each year, and should be run in cooperation with other partners to maximise means available and impact (e.g. media partners). The yearly budget for campaigns is set at follows:

Year 1	120.000
Year 2	420.000
Year 3	420.000
Year 4	220.000
Year 5	120.000

The higher budgets in the second and third year are justified by the need to make the existence of the CE and Liaison office networks known early in the process;

- a budget to cover miscellaneous communication actions included in the plan. This can go from paying a fee to someone making a presentation at a public event, or sponsoring an event where the plan's communication objectives can be leveraged, or translations of material in order to have good practice material available in both national languages. The yearly budget for this is set at 20.000 euro.

All three measures above should be considered as interlinked.
The staff under measure 3.1 and 3.2 will be communication specialists, and therefore also participating in the management of the actions paid for under measure 3.3.
Measure 3.3 budget should be considered as a budget available to the management of the plan to reach the communication objectives. Its use will be defined in the yearly communication plan.

Measure 4: Patient empowerment
Measure 4.1.a – Instruments and tools to empower patients
Measure 4.1.b – Help line
Measure 4.1.c – Responsibility to inform, also on adherence

Responsibilities and costs will be at the level of the network of CEs, including the CHG and the liaison officers

on the one hand and the patient organisations on the other hand. Costs linked to it can therefore be part of 8.1, or of 4.2.

Measure 4.2: Enforceable patient participation at level of Centres

To cover the costs of this measure we propose to earmark a fund that would be used to cover the value delivered by patients and patient organisations involved in this process. To avoid potential conflicts of interest, this could be a fund that is managed centrally (by the National Platform or an independent structure). Each formal agreement signed between a CE with a patient organisation could, based on the number of patients and the agreed 'service', be subsidised through this fund (after eligibility check by the staff).

The National Platform could contract a specialised consultant to assist in this process and ensure that similar standards and tools are used in the different CEs.
An additional advantage of having this managed centrally is that the information will then also be available centrally and be used for the monitoring and evaluation of the plan.

The initial budget proposed is 120.000 euro/year. This budget is however increasing over time as the expectation is that the value of the patient contribution to the care of patients will be appreciated and that more will be asked to patients and their patient organisations over time [92]. This is also the case if the working group proposed in measure 4.3 leads to more initiatives.

The budget proposed therefore increases to 200.000 € in the fifth year.

Measure 4.3: Working group on cooperation

The costs of this measure are part of the management cost as it would be one of the working groups managed under the national plan.
This working group could however lead to additional costs as an ambition of the working group is to define the role patient organisations can play in the care system and as a consequence, the level of support needed to fulfil that role (see also above in 4.2).

Measure 4.4: Ensure the development of an instrument for rapid communication of medical need in case of emergency

The initial cost for the policy work at EU level falls under the budget of the National Platform. The investment cost linked to a national set up in case the European approach is not leading to results, is estimated at 50.000 € and included as an investment in year 1. It could take the form a service contract (typically for service design), coupled with a working group who would define the terms of reference and monitor the service contract implementation. If sufficient progress is made at EU level, this budget post can be omitted.

Measure 5.1: Integration of education and teaching about rare diseases (and orphan drugs)

A budget of 50.000 euro/year is foreseen for:

- the creation of education and training material;
- the cost of sending patient organisation representatives to give part of these trainings, including the cost of training these patients in giving professional level trainings.

This budget should normally come from the regions and could ideally be managed by the National Platform to be allocated on a project basis.

92 *This could also lead to a transfer of funds from CEs to POs, therefore with a zero effect on the budget.*

Measure 5.2: The introduction of rare diseases in the continuous medical education (CME) of general practitioners and approved in the current accreditation system by RIZIV/INAMI.
A budget of 30.000 euro/year is foreseen. This budget will be managed by the National Platform and will be used to finance courses organised by third parties (networks of Centres, or others) organising these courses.

Measure 6.1: Allow DNA samples to be tested abroad
The budget impact of this measure will probably be between 0.5 and 1 million Euro.

The basis of this calculation is an inventory done by the eight Centres for Human Genetics in Belgium for the year 2007: 846 tests were performed abroad at a cost of 430.000 Euro.

The lower end of the estimate is based on 1.000 samples/year at an average cost of 500 euro/sample. The higher end of the estimate is based on an increase in volume to 2.000 and a similar average cost/test/sample.

This measure should be combined with measures on standardisation of quality and as part of this, of purchasing decisions for tests. The procedure to choose suppliers and negotiate prices with these suppliers needs to be 'coordinated' to ensure both the quality of the test and service (e.g. only accredited labs) as the cost (price charged, cost of transport taken into account).
If this is not done, neither the cost to the health insurance system nor the quality of the service to patients will be optimal.

This measure was included and approved as part of Phase 1 of the Plan. The budget foreseen, which will be part of the financing package of the CHG, is 550.000/year. In the Plan we have included an increasing budget, as we expect different factors to have an influence on the volume (an increase in volume), which will partly offset by a gradually reduced cost of tests (due to lowering prices and better purchasing). These factors are:

- the success of the Plan, leading to more patients passing through the system;
- the increased transnational cooperation and specialisation of labs, leading to more volume going to other countries (partly offset by increasing income of our own CHG whose revenue from tests performed for foreign patients is expected to increase).

Measure 6.2: non-DNA testing access and reimbursement
Not enough information could be collected during the preparation of this measure to make an estimate of the budget impact.
This measure potentially covers on the one hand a large number of technologies and tests, but on the other hand, a small number of patients.
The budget included in the plan is therefore set at 1/3rd of the cost earmarked for the DNA tests sent abroad, or 330.000 euro in the fifth year.

Measure 7.1: Information system on clinical trials, compassionate use and medical needs programmes
The implementation of this measure should normally fall under the remit of the FAHMP.
The investment related to the measure is put at zero in the table, but it is however significant, and will probably lead to switches in the way resources are used within the FAHMP.

Measure 7.2: Adapt existing legislation to increase transparency and availability of information from compassionate use and medical need programmes

Measure 7.3: Awaiting an adaptation of the EU clinical trials Directive, Belgium should proactively apply the so-called 'Voluntary Harmonised Procedure' whenever a request to launch a clinical trial in Belgium for an orphan drug

Measure 7.4: Improvements are possible to the way ethics committees are coming to a single opinion in the case of rare diseases where by definition no alternative treatments are available to the patients

All the measures above are not generating any direct costs or budget impacts.

Measure 7.5: Academic (non-commercial) clinical trials for rare diseases should be stimulated financially and made more visible

No specific investment is included in the budget overview table. The proposed stimulation could be financed using the funds earmarked for area 9 (research – particularly translational research). More innovative financing mechanisms could also be considered: public-private partnerships, risk or seed capital instruments.
The increased visibility should be achieved through actions under the communication plan. The budget impact or cost is therefore included under that measure.

Measure 7.6: The role of the Special Solidarity Fund should be redefined

The measure as such is not expected to generate costs. One of the potential decisions suggested might however have an impact on the expenditure of the SSF. If the recommendation is followed to adapt the interpretation of the rules, this will lead to more expenditure. Estimating this impact, in case this recommendation is taken up, is however impossible due to the nature of the SSF: we are talking about individual patient cases and exceptions. Treatment costs can also range from small to very expensive. No budget impact was therefore included as this would be highly speculative.

Measure 7.7: Ensure that materials for compounding used to treat rare diseases, can be used legally

This measure will generate a small cost to have batches of compounding material certified so that they can be used legally. A budget of 10.000 euro has been earmarked, which could be handled by the Platform.

Measure 7.8: Early access and early reimbursement of orphan drugs

The budgetary impact of the measure is difficult to estimate, as it depends on the actual behaviour of the pharmaceutical companies. The system should however make Belgium more attractive to introduce new medicines faster on the market.
Taking into account the experience up to now with orphan drugs and the expectation that approximately 5 to 10 new drugs would enter the market each year, this measure 'could' generate an increase for the orphan drugs cost of 3.5 to 7 million euro/year (or 6 to 12 % taking 2008 as a basis). This additional cost could be fading off over time, but is budgeted as a permanent extra cost.
This cost was part of Phase 1 measures and approved. A budget of 3.5 M euro was foreseen for 2011. This budget has been kept over the full period of the Plan as an expected 'net increase' compared to a situation without the measure.

Measure 7.9: Enhanced role for colleges for orphan drugs

The budget impact for this measure in the overview table is zero.

This measure will cost through the fees that have to be paid to experts participating in Colleges and through the costs for the administrative support. These costs should be higher with the proposed enhanced role than they are at the moment and are part of the budget (staff, overhead) of RIZIV/INAMI.

Measure 7.10: Responsible off-label use of drugs should be possible to treat patients with rare diseases under specific conditions.

The potential budgetary impact of this measure is very difficult to estimate. The fact that off-label use becomes more transparent does not necessarily mean the cost to the health insurance budget will be higher. Better treatment should also lead to savings in the longer term. Still, a medium term impact will probably be an increase of requests at the level of the Special Solidarity Fund, and therefore an increase of costs for the health insurance. An increase of 10% of the expenditure of the SSF as a consequence of this measure, could mean an amount of up to 1 million euro/year, based on expenditure in the last five years. Although this estimate is highly speculative, it was included in the budget impact estimate as a gradually increasing cost up to the fifth year.

Measure 7.11: Support home treatment for orphan drugs under clear conditions

Budget impact: home treatment is expected to be cost-neutral to slightly less costly than hospital treatment.

Measure 7.12: Stimulate patient adherence through a set of initiatives

Budget impact: costs will mostly be linked to setting up the measure itself which are part of the budget for the proposed measure for a communication plan. An increase in adherence should lead to higher costs to the health insurance budget, but these costs were foreseen at the moment of taking the reimbursement decision.

Measure 7.13: Belgium to take a leading role in a number of European issues related to access to treatment for patients with a rare disease

These measures should not generate direct budgetary impacts and in the longer term, rather net savings. It does however imply continued attention at policy level and resources to actively participate and eventually lead EU level initiatives. It might make sense to earmark a budget to be able to contract out some tasks, e.g. to write background papers to ease decision-making, or organize EU-level events to facilitate the decision-making process.

Measure 8.1: Creation of a Care coordination function (at the level of CEs)

This measure proposes that CEs would define not only a medical roadmap for the individual patient, but a total care roadmap to ensure that the paramedical and social needs of patients and their family are taken into account.

The central element in the measure is the creation of a care coordination function in each CE.

Because of the expected small size of the CEs, this is expected to be a part-time function at the level of the individual centre. As it is expected this function will be clustered between 2-3 centres within the same hospital, and because of economic reasons, it is proposed the care coordination is split over two posts or persons, one of a more managerial nature, taking the coordination tasks, the links with senior medical staff both in and outside the centre, and a second person with a more advisory role, concentrating on the individual assistance and advice to the patient.

The function of care coordination has various impacts to be taken into account when calculating the budget impact, whether positively or negatively:

- the function will save time of senior medical staff as the function takes care of relationships with a

decentralised network, and of coordination between various medical and non- medical disciplines. Compared to the present situation, where such role is often devoted to senior medical staff, this will mean a transfer of time spent leading to an expected better service to the patient at a lower overall cost for the time spent. This expected effect is one of the elements justifying the expected 'low' average cost/patient treated in a CE and included in the budget of measure 1.1.;

- the function itself includes a number of elements part of them not linked to the number of individual patients to be treated, and part linked to the number of patients treated. These are summarised below in a table.

Tasks not linked to number of patients	Tasks linked to the individual patient
—Build and manage a network with medical and paramedical professionals inside and outside the CE, including with pathology based patient organisations —Monitor the quality of service and caretaking (globally) for the cohort of patients followed by the CE —Report to the National Platform on activities of the centre, particularly with regard to cooperation —Monitor the economic aspects of the global patient pathway, including the medical aspects; provision of information on a yearly basis for the monitoring of the reimbursement level for the CE.	—Ensure liaison between CE and others involved in the caretaking of the patient (GP, specialist, foreign centre,…) —Participate in the individual needs assessment of patients, with responsibility on the coordination and the social aspects —Provide the necessary information and advice with regard to individual social needs and rights through own staff, social service of the hospital —Assist the patient at individual level to establish and develop relationship with caretakers outside the centre; this includes patient organisations —Register the patient in the national and disease specific registry

The majority of tasks being linked to the number of patients, the financing of the function is proposed to be calculated based on the number of patients treated within the centre. Although this would be the principle used for defining the financing, the recommendation to hospitals is to combine the function over groups of CEs. Hospitals having only one CE, should therefore consider cooperation with nearby hospitals to ensure the function is taken up in cooperation.

The proposed contribution per patient would be estimated based on the following principles:

- for new patients (definition of global care pathway): 0,75 person/day of both a manager and an advisory function;
- for patients being followed by the centre: 0,25 person/day of the manager and 0,5 person/day of the advisor.

The tariff calculation for a manager function is based on:

- use of time (220 working/days/year): 20 days non-productive (training, sick leave,…); 80 days on global tasks not directly linked to individual patients and 120 days on tasks linked to individual patients;
- direct cost of the staff member including overhead of 90.500 euro/year[93].

93 *This cost is based on the barema of RIZIV/INAMI for a psychologist (average of full direct salary cost for 15 and 25y experience), with an overhead (100/84).*

The tariff calculation for the advisor function is based on:

- use of time (220 working/days/year): 20 days non-productive (e.g. training, sick leave,…); 200 days on tasks linked to individual patients;
- direct cost of the staff member including overhead of 73.000 euro/year[94].

Based on these principles, a CE would receive following budgets:

- for 'new' patients: 839,38 euro;
- for 'old' patients: 371,04 euro.

This would be valid for patients followed in the CE, but also for patients that are followed in CEs in other countries, primarily by the care coordinators that are linked to the Liaison centre function within a university hospitals.

For all CEs together, including patients followed in CEs outside Belgium, the estimate in year 5 would be 8,8 M euro.

The need to create critical mass:

Based on experience both in and outside Belgium, one of the important risks with the creation of these functions is the high turnover in staff. This risk is mainly the consequence of the part time nature, leading to regular movement of people.

It is therefore recommended to CEs and the hospitals in which they are hosted, to cluster 2 to 3 CEs to have a team of two full times in charge of this function; and to ensure the persons in charge within the hospital work as a team, exchanging experience and information, in order to be able to back each one up in case of absence and pass on knowledge when staff move out of the function.

The need to monitor actual time spent and impacts

The creation of this global care coordination function is an innovation and one of the most important measures proposed. The potential impact is very significant, but due to the innovative nature, implementation needs to be monitored very closely. This also applies to the actual time spent by the staff. It is therefore proposed that the staff in charge of this function would keep timesheets. These timesheets can be used to exchange experiences among the CEs, to agree on standards of service, and to revise the estimates made above.

Measure 8.2: To facilitate the access to specialized help, to simplify the administrative procedures

Some administrative savings are expected at the level of the sickness funds. The management of specific needs or not encountered needs until now will have a certain cost. In some cases, the measures and the rights provided by the listings will only concern a few or a limited number of people.

Measure 9.1: Research projects on rare diseases should be made identifiable and traceable within (national) research support programs

There are no direct costs involved. Costs for follow up of this measure fall under the responsibility of the National Platform and Orphanet Belgium (for the extraction of data and adding them into Orphanet).

Measure 9.2: Increase national support to E-rare

There are no direct costs to the healthcare budget since the financing involves a transfer of existing research funds towards E-Rare.

94 *This cost is based on the RIZIV/INAMI barema for a nurse with 15y experience including overhead (100/84)*

Measure 9.3: An impulse program for research on rare diseases
An investment of 9 Million euro in research for a programme implemented over the full period is recommended to have an impact.

Measure 9.4: Identification of unmet medical needs
This should ideally be an EU-level initiative and the costs would therefore be carried by the EU-level. No costs were included in the overview table.

Measure 9.5: Public funds are available for translational research
An investment of 3 Million euro is recommended as a minimum.

Measure 10: Management of the Belgian Plan
Independently of the practical solution decided for the management of the Belgian Plan, there are a number of functions and related costs which are described in this section. The assumption taken is that there would be a type of a 'Platform' with its own staff or with staff that is seconded from other institutions to take up the function and roles.

The type of costs included under management include:
- leading role taken by Belgium on RD issues (measure 7.13);
- management of the measures in area 4;
- manage the networking at national and EU level, including the funds earmarked for this activities (measures 1.4 and 1.5);
- hiring consultants to set-up measures or new processes, including defining standards of services;
- organise trainings for staff of CEs and particularly staff in charge of global care coordination (measure 8.1) to ensure common standards of service are used throughout the network.

The total budget proposed for this type of costs is 100.000/euro/year, taking into account that this budget can be used to cover costs of events or initiatives that are not falling within another budget. 30% of this budget should be earmarked for the last activity mentioned above (training of staff of centres of expertise).

Mid-term and final evaluation of the Plan:
Two budgets of 250.000 € are foreseen for evaluations (mid-term and final). The mid-term budget is split over years 2 and 3. The final evaluation is part of the year 5 budget.

The Platform can only play its role if it has a staff that would perform a number of functions. The list below summarises these functions and is non-exhaustive.
- participate in the yearly review of economic aspects of the CE functioning; this is mainly the facilitation of the process within the CEs, including passing on best practice and suggesting improvements;
- supervise the yearly customer satisfaction evaluations performed at the level of CEs and in cooperation with patient organisations;
- monitor the functioning of the liaison function in all university hospitals;
- manage the functioning of the working groups and act as their secretariat;
- manage the implementation of measure 8.2: this could lead to the creation of specific working groups, but not necessarily;
- ensure the liaison with the various stakeholders, which includes the preparation of the decision-making process and the monitoring of the implementation of decisions taken. This includes decisions linked to launching calls for new CEs, the definition of care and therapeutic pathways;

- supervise the persons in charge of communication, and manage the communication plan, including the coordination of the four main components and the cooperation with stakeholders, particularly the patient organisations;
- manage the evaluations;
- manage the national and international networking;
- manage measure 7.13 – leading role at EU level;
- manage the relationships with Patient Organisations including the implementation of measure 4.2.

To perform these functions, it is proposed that the Platform would have a staff of four FTE.
One of these persons would be a secretary general. This person should act as the manager of the National Plan. We recommend this person is hired for the function.

Another of the team members should be a communication specialist to manage the communication plan, the portal and cooperation agreements with stakeholders related to communication objectives.
The two other staff members would work half time on the task described under measure 1.1 to 'review the economic aspects of the CE functioning; this is mainly the facilitation of the process within the CEs, including passing on best practice and suggesting improvements'.

The three staff members who would assist the secretary general can be hired, like they can be seconded from existing institutions or be covered through service contracts with third parties. Independently of this choice, the economic cost will be similar and is included in the budget of the national plan.

Cost for 4 staff members (one secretary general, two professionals, one organisational assistant), including a small overhead: 400.000 euro/year.
This staff and the performance of their tasks are expected to generate a cost of up to 200.000 euro/year. This includes the cost of 100.000 euro mentioned under measure 1.1 to cover costs of review panels for CEs (economic/cost aspects and best practice). The remainder of the budget would mainly be used to finance meetings (e.g. of working groups).

Measure 11.1: Transparency of pricing
There are no direct costs involved when the study proposal is taken up by the KCE or the European Commission.

Measure 11.2: Citizens consultations on rare diseases and orphan drugs
Organising such citizens consultations is a cost, both in terms of staff time, physical costs, reimbursements paid to the participants, facilitation, reporting, translations, etc. If the suggested National Platform gets the responsibility to organise such citizens consultations, this would have implication in the need for staff and in a budget for the management of the process. This cost is estimated at 75.000 euro for each cycle.

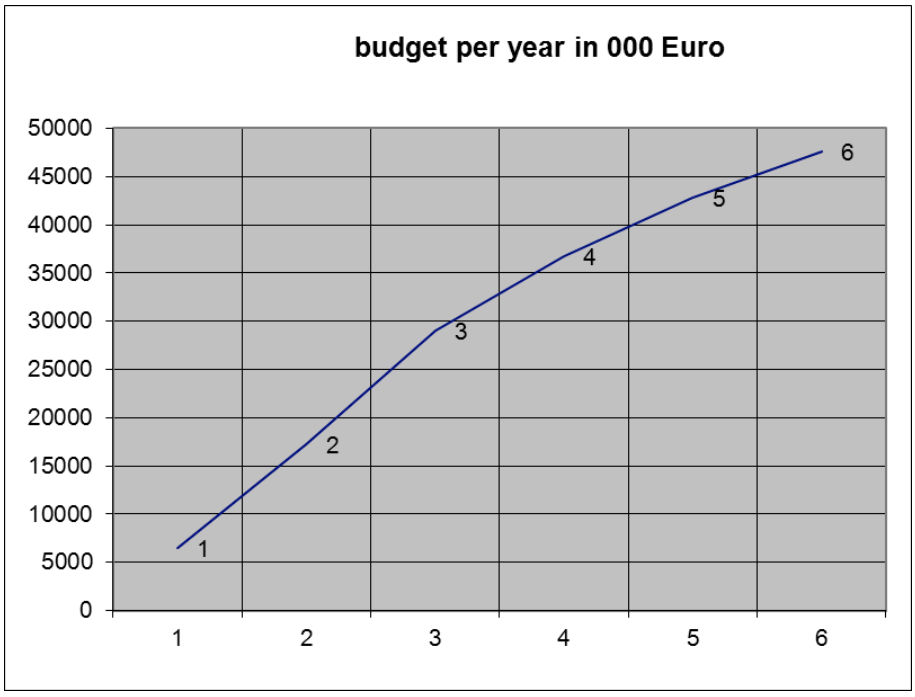
Conclusions and overview

An overview table is attached to this document that includes a proposal of spread of investments over the duration of the Plan.

The chart below gives the evolution of the budget impact over time. Year 1 is 2011 and includes budgets that are planned to be spent in 2011 as they are part of the approved RIZIV/INAMI budget for 2011.

The main conclusions with regard to the overall figures are:

- the total cost of the plan over five years is 174 million euro or an average 35 million euro/year;
- two measures generate 68% of the total budget impact: the creation of centres of expertise and the function of care coordination;
- the total budget impact can be split into two categories:
  - ◇ one off or investment costs. These costs will be incurred during the five years, but will stop with the end of the plan period. This represents 17 million euro or 10% of the total;
  - ◇ costs or budget impacts that will become 'regular'. This budget impact surpasses 44 million euro/year in the fifth year;
- measures are not necessarily independent of each other. It does e.g. not make much sense to invest 100 million euro over five years to create centres of expertise on many rare diseases, and not plan a budget to make these centres known to the different target groups. The 1.7 million euro budget for communication campaigns should be considered in this context;
- the budget size of some measures also defines the ambition and therefore the impact. Examples are the resources invested in creating registries (2 million) or in research (12 million). Investing more resources in both areas would make sense to have a higher impact, but on the other hand, these contributions made by Belgium should be considered in a EU context of sharing resources and investments to reach together a higher impact in terms of diseases covered, patients involved and new treatments reaching the market.



The table below is a synthetic version of the full table, as budgets are grouped by domain of the proposed measures. The figures include 2011.

Areas	value in 1.000€	%
Area 1. Expert centres	98.914	55,0%
Area 2. Registries	3.250	1,8%
Area 3. Communication	2.550	1,4%
Area 4. Patient empowerment	830	0,5%
Area 5. Training of health professionals	400	0,2%
Area 6. Improving access to diagnosis	5.830	3,2%
Area 7. Improving access to treatment	23.450	13,0%
Area 8. Comprehensive care	28.800	16,0%
Area 9. Stimulating research	12.000	6,7%
Area 10. Management of the Plan	3.700	2,1%
Area 11. Ethics & Governance	150	0,1%
Total	**179.874**	

Overview of potential measures - estimated budget impact and cost for a Belgian Plan Rare Diseases (in 1.000€)								
Areas	**Potential measures**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**Total**
Area 1. Improving the quality of diagnosis, therapy and patient management by setting up expert centres and expert networks	1.1. Creation of Centres of Expertise (CE)	2014	7000	14000	19000	24000	27000	93014
	1.2. Strengthen the role of the Centres of Human Genetics (CHG)		200	200				400
	1.3. Liaison Network RD	0	750	1000	1000	1000	1000	4750
	1.4. Networking between Centres of Expertise at national level		50	50	50	50	50	250
	1.5. Networking between Centres and pheripheral care services		50	50	50	50	50	250
	1.6. Networking at European and international level		50	50	50	50	50	250
Area 2. Codifying and inventorying rare diseases	2.1. National Belgian Registry for Rare Diseases - development costs (generic and disease specific)	200	500	500	300	300	200	2000
	2.2. Belgian Registry for Rare Diseases - running costs		200	250	250	250	300	1250
Area 3. Information and communication	3.1. Creation of a national portal website with actual and validated information	100	100	100	100	100	100	600
	3.2. Support for Orphanet Belgium	100	30	30	30	30	30	250
	3.3. Communication Plan		200	500	500	300	200	1700
Area 4. Patient empowerment	4.1. Empower patients in their relation to health care professionals							0
	4.2. Enforceable patient participation at the start up, functioning and evaluation of Centres of Expertise		120	120	160	180	200	780

	4.3. Improvement of the collaboration between patient organisations							0
	4.4.medical passport or other instrument for emergency medical information		50					50
Area 5. Training and education of health professionals	5.1. To integrate education and teaching about rare diseases (and orphan drugs)		50	50	50	50	50	250
	5.2. Rare diseases in continous medical education (CME)		30	30	30	30	30	150
Area 6. Improving access to and financing of diagnosis	6.1. Change the system to allow DNA-samples to be tested abroad	550	600	700	800	900	1000	4550
	6.2. Access and reimbursement of non-DNA testing and development of such technologies in Belgium		200	200	250	300	330	1280
Area 7. Improving access to and financing of treatment	7.1. Launch an information service on clinical trials, compassionate use and medical need programmes							0
	7.2. Adapt existing legislation to increase transparency and availability of information from compassionate use and medical need programmes							0
	7.3. Awaiting an adaptation of the EU clinical trials Directive, Belgium should proactively apply the so-called 'Voluntary Harmonised Procedure' whenever a request to launch a clinical trial in Belgium for an orphan drug							0
	7.4. Improvements are possible to the way ethics committees are coming to a single opinion in the case of rare diseases where by definition no alternative treatments are available to the patients							0

Overview of potential measures - estimated budget impact and cost for a Belgian Plan Rare Diseases (in 1.000€)								
	7.5. Academic (non commercial) clinical trials for rare diseases should be stimulated financially and made more visible							0
	7.6. The role of the Special Solidarity Fund should be redefined							0
	7.7. Ensure that materials for compounding used to treat rare diseases, can be used legally		10	10	10	10	10	50
	7.8. Setting up a system for early access to orphan drugs including early temporary reimbursement	3500	3500	3500	3500	3500	3500	21000
	7.9. Colleges for orphan drugs have proven to be a good practice. Their role and use could be enhanced and strengthened for a higher impact.							0
	7.10. Responsible off-label use of drugs should be possible to treat patients with rare diseases under specific conditions.							0
	7.11. Support home treatment for orphan drugs under clear conditions							0
	7.12. Stimulate patient adherence through a set of initiatives		0	200	500	700	1000	2400
	7.13. Belgium to take a leading role in a number of European issues related to access to treatment for patients with a rare disease							0
Area 8. Comprehensive care of the patient	8.1. To simplify the access to measures concerning diagnosis and coordinated treatments, to propose the assistance of a 'rare disease care coordinator'		2000	4000	6500	7500	8800	28800
	8.2. To facilitate the access to specialized help, to simplify the administrative procedures							0

Area 9. Stimulating research on rare diseases	9.1. Research projects on rare diseases should be made identifiable and traceable within (national) research support programs							0
	9.2. Increase national support to E-rare							0
	9.3. An impulse program for research on rare diseases		1000	2000	2000	2000	2000	9000
	9.4. Identification of unmet medical needs							0
	9.5. Public funds are available for translational research			750	750	750	750	3000
Area 10. Management of the Plan	10.1. Staff related costs		300	400	400	400	400	1900
	10.1 costs linked to the functioning of Platform (and working groups)		200	250	250	300	300	1300
	10.1. mid-term and final evaluations			125	125		250	500
Area 11. Ethics	11.1. Transparency of pricing							0
	11.2. Citizens consultations on rare diseases and orphan drugs				75	75		150
TOTAL		**6464**	**17190**	**29065**	**36730**	**42825**	**47600**	**179874**

Annex 9. Composition of the Management Committee of the Fund for Rare Diseases and Orphan Drugs

President and Vice-President

Cassiman Jean-Jacques, Prof. dr. emeritus

Abramowicz Marc, représentant du Haut Conseil d'Antropogénétique

Members

Honorary member: Avontroodt Yolande, voorzitster Algemeen Beheerscomité RIZIV/INAMI

Bogaert Marc, voorzitter College van Geneesheren voor Weesgeneesmiddelen bij het RIZIV

Bours Vincent, chef de service Département Génétique ULg

Bruyninckx Klaartje, stafmedewerker Vlaams Patiëntenplatform (VPP)

De Baere Lut, voorzitster Rare Diseases Organisation (RaDiOrg.be)

De Groof Vera, afgevaardigde Intermutualistisch College (tot 01/12/2009)

De Ridder Ri, directeur-generaal dienst voor geneeskundige verzorging RIZIV

Dooms Marc, vertegenwoordiger Belgische Vereniging van Ziekenhuisapothekers

Eyskens François, diensthoofd Provinciaal Centrum voor Metabole Opsporingen Antwerpen en kliniekhoofd pediatrie UZA

Gerits Pol, adjunct van de Directeur-generaal Organisatie Gezondheidszorgvoorzieningen, FOD Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu

Jansen Herwig, coördinator Belgisch Mucoviscidose Register, Afdeling Epidemiologie WIV

Leto Celine, conseillère cabinet de la Ministre Laurette Onkelinx. (vanaf 01/10/2009)

Lhoir André, représentant du FAGG et membre belge du COMP (EMA)

Maes Sophie, experte Cabinet de la Ministre Laurette Onkelinx

Musch Greet, directeur-generaal DG PRE FAGG

Neels Leo, directeur Pharma.be

Nelis Gustaaf, vertegenwoordiger Intermutualistisch College

Neyt Mattias, expert Economic Analysis, Federaal Kenniscentrum voor de Gezondheidszorg (tot 30/09/2009)

Poppe Bruce, Klinisch geneticus Centrum Medische Genetica UZ Gent

Sokal Etienne, Cliniques universitaires Saint-Luc, Unité de gastroentérologie et hépatologie pédiatrique

Sterckx Claude, président de la Ligue des Usagers des Services de Santé (LUSS)

Sumkay François, représentant Collège Intermutualiste

Tambuyzer Erik, hoofd werkgroep Zeldzame Ziekten en Weesgeneesmiddelen Pharma.be, senior vice president Global Public Policy Genzyme

Tassignon Marie-José, voorzitster Raad van de Universitaire Ziekenhuizen van België

Van Hul Chris, vertegenwoordiger Intermutualistisch College

Vandensande Tinne, adviseur Koning Boudewijnstichting

Substitutes

Aubry Chris, bestuurslid RaDiOrg.be

Gendreike Viviane, présidente suppléante du Collège des médecins-directeurs INAMI

Haucotte Geneviève, secrétaire du Comité scientifique des Maladies chroniques et Affections spécifiques INAMI

Pypops Ulrike, bestuurslid RaDiOrg.be

Herman Van Eeckhout, adjunct algemeen directeur Pharma.be

Weeghmans Ilse, coördinator VPP

Annex 10. Composition of the Working Groups of the Fund for Rare Diseases and Orphan Drugs

WORKPACKAGE 1:

National Registry, Disease specific databases and European collaboration

WORKING GROUP

President

Jansen Herwig, coördinator Belgisch Mucoviscidose Register, Afdeling Epidemiologie, Wetenschappelijk Instituut Volksgezondheid

Members

- Bours Vincent, chef de service Département Génétique, ULg
- Cassiman David, verantwoordelijke zorgprogramma Metabole Ziekten, UZ Leuven
- De Laet Corinne, chef de Clinique Adjoint Hôpital Universitaire des Enfants Reine Fabiola, HUDERF, Bruxelles
- Delcroix Marion, kliniekhoofd Interne geneeskunde Pneumologie, UZ Leuven
- De Meirleir Linda, researcher Faculteit Geneeskunde en Farmaceutische Wetenschappen – Centrum voor Metabole Aandoeningen,VUB (tot juni 2010)
- Pypops Ulrike, bestuurslid RaDiOrg.be
- Ribaï Pascale, neurologist and clinical geneticist, Clinique Edith Cavell Bruxelles – Hôpital du Beau-Vallon Namur
- Swinnen Elfriede, wetenschappelijk medewerker Centrum Menselijke Erfelijkheid KULeuven – Orphanet België
- Vincent Marie-Françoise, Service de Biochimie médicale, Laboratoire des maladies métaboliques et centre de dépistage néonatal, Cliniques universitaires Saint-Luc

WORKPACKAGE 2:

Identifying hidden non-medical costs for patients/ towards a roadmap for patients

WORKING GROUP

President

Sterckx Claude, président Ligue des Usagers des Services de Santé (LUSS)

Members

- Aubry Chris, bestuurslid RaDiOrg.be, Coördinator Vaardigheidscentrum, Faculteit Geneeskunde, KULeuven
- Cassiman Jean-Jacques, Prof. dr. emeritus
- De Groof Véra, Intermutualistisch College (tot december 2009)
- Detavernier Luc, expert Matières régionales et communautaires, Union Nationale des Mutualités Libres
- Dooms Marc, apotheker UZ Leuven Campus Gasthuisberg – Belgische Vereniging van Ziekenhuisapothekers
- Dupré Christian, Service francophone pour Handicapés, COCOF
- Haucotte Geneviève, secrétaire du Comité scientifique des Maladies chroniques et Affections spécifiques INAMI
- Hens Evelyne, stafmedewerker Nationaal Verbond van Socialistische Mutualiteiten
- Jageneau Ingrid, administratrice RaDiOrg.be
- Minet Cécile, Centre de Génétique humaine, Institut de Pathologie et de Génétique, Gosselies
- Nelis Gustaaf, Intermutualistisch College
- Nouwen Annie, Vlaams Agentschap Personen met een Handicap (VAPH)
- Ribaï Pascale, neurologist and clinical geneticist, Clinique Edith Cavell Bruxelles – Hôpital du Beau-Vallon Namur
- Swinnen Elfriede, Wetenschappelijk medewerker Centrum Menselijke Erfelijkheid KULeuven – Orphanet Belgium
- Vandenbroucke Nathalie, stafmedewerker Vereniging Personen met een Handicap VFG
- Van Hul Chris, Vertegenwoordiger Intermutualistisch College

WORKPACKAGE 3:

Information for patients, health professionals and the public

Patient empowerment.

WORKING GROUP

President

Bruyninckx Klaartje, stafmedewerker Vlaams Patiëntenplatform (VPP)

Members

- Aubry Chris, Bestuurslid RaDiOrg.be, Coördinator Vaardigheidscentrum, Faculteit Geneeskunde, KULeuven
- Blaumeiser Bettina, Department of Medical Genetics UA
- Claes Patrick, projectmedewerker Nema vzw
- Colaert Karen, Vlaams Agentschap Zorg en Gezondheid
- De Baere Lut, voorzitter Rare Diseases Organisation (RaDiOrg.be) (Fase I)
- De Groof Vera, afgevaardigde Intermutualistisch Agentschap (tot 01.12.2009)
- De Kegel Tim, secretaris-generaal Pharma.be (tot 30.09.2009)
- De Tavernier Luc, expert Matières régionales et communautaires, Union Nationale des Mutualités Libres
- Dooms Marc, apotheker UZ Leuven Campus Gasthuisberg – Belgische Vereniging van Ziekenhuisapothekers
- Gerits Pol, adjunct van de Directeur-generaal Organisatie Gezondheidszorgvoorzieningen, FOD Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu
- Mores Benoît, Kankercentrum
- Sznajer Yves, Centre de génétique humaine, UCL
- Swinnen Elfriede, Wetenschappelijk medewerker Centrum Menselijke Erfelijkheid KULeuven – Orphanet Belgium
- Vrints Raf, vertegenwoordiger Pharma.be

WORKPACKAGE 4:

Centres of Competence, Centres of Expertise, and National Collaboration (Including Neonatal Screening)

WORKING GROUP

President

Cassiman Jean-Jacques, Prof. dr. emeritus

Co-president

Eyskens François, diensthoofd Provinciaal Centrum voor Metabole Opsporingen Antwerpen en kliniekhoofd pediatrie UZA

Members

- Abramowicz Marc, chef de Clinique Centre de Génétique Humaine, Hôpital Erasme – ULB
- Bours Vincent, chef de service Département Génétique, ULg
- Calcoen Piet, medisch directeur DKV
- Dahan Karin, Centre de Génétique humaine, Institut de Pathologie et de Génétique, Gosselies
- De Baere Lut, voorzitter Rare Diseases Organisation RaDiOrg.be
- Debled Sabine, Direction de la Promotion de la Santé, Ministère de la Communauté française
- De Meirleir Linda, researcher Faculteit Geneeskunde en Farmaceutische Wetenschappen – Centrum voor Metabole Aandoeningen, VUB
- Gerits Pol, adjunct van de Directeur-Generaal Organisatie Gezondheidsvoorzieningen, FOD Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu
- Haucotte Geneviève, secrétaire du Comité scientifique des Maladies chroniques et Affections spécifiques, INAMI

- Nassogne Marie-Cécile, chef de service dépt. Neurologie Pédiatrique, Cliniques Universitaires Saint-Luc, Bruxelles
- Poppe Bruce, Centrum Medische Genetica UZ Gent
- Remiche Gauthier, Dépt. Neurologie, Maladies neuromusculaires et Neurophysiologie, Hôpital Erasme, Bruxelles
- Swinnen Elfriede, wetenschappelijk medewerker Centrum Menselijke Erfelijkheid KULeuven, Orphanet Belgium
- Tassignon Marie-José, voorzitster Raad van de Universitaire Ziekenhuizen van België
- Vandenbulcke Pieter, afgevaardigde Vlaams Agentschap Zorg en Gezondheid
- Verellen-Dumoulin Christine, directeur de l'Institut de Pathologie Génétique Gosselies
- Vincent Marie-Françoise, Service de Biochimie médicale, Laboratoire des maladies métaboliques et centre de dépistage néonatal, Cliniques universitaires Saint-Luc
- Westhovens René, ondervoorzitter Belgische Vereniging Reumatologie, UZ Leuven

WORKPACKAGE 5:

Access to and financing of diagnosis, medication, treatment and patient management

WORKING GROUP

President

Tambuyzer Erik, hoofd Werkgroep Zeldzame Ziekten en Weesgeneesmiddelen bij Pharma.be

Co-president

Bogaert Marc, voorzitter College van Geneesheren voor Weesgeneesmiddelen bij het RIZIV – Heymans Instituut UGent, Vakgroep Farmacologie

Members

- Aubry Chris, bestuurslid RaDiOrg.be
- Delcroix Marion, kliniekhoofd Interne geneeskunde Pneumologie, UZ Leuven
- De Meirleir Linda, researcher Faculteit Geneeskunde en Farmaceutische Wetenschappen – Centrum voor Metabole Aandoeningen,VUB
- Dooms Marc, apotheker UZ Leuven Campus Gasthuisberg - Belgische Vereniging van Ziekenhuisapothekers
- Eyskens François, diensthoofd Provinciaal Centrum voor Opsporing van Metabole Aandoeningen Antwerpen – kliniekhoofd pediatrie UZA
- Gendreike Viviane, présidente suppléante du Collège des médecins-directeurs INAMI
- Haucotte Geneviève, secrétaire du Comité scientifique des Maladies chroniques et Affections spécifiques, INAMI
- Hermans Cédric, Haemostasis and Thrombosis Unit, Haemophilia Clinic, Cliniques universitaires Saint-Luc, UCL
- Hermans Céline, pharmacienne en charge des dossiers du Collège des Médicaments Oprhelins, INAMI
- Matthijs Gert, hoofd Laboratorium Medische Genetica KUL
- Musch Greet , directeur-generaal DG PRE FAGG
- Nelis Gustaaf, Intermutualistisch College
- Pypops Ulrike, bestuurslid RaDiOrg.be
- Stoop Hilde, afgevaardigde Werkgroep Zeldzame Ziekten en Weesgeneesmiddelen Pharma.be/Bio.be
- Stryckman Françoise, conseiller Scientifique Remboursements, Direction Politique des Médicaments Pharma.be
- Sumkay François, Collège Intermutualiste
- Van Hul Chris, vertegenwoordiger Intermutualistisch College

WORKPACKAGE 6:

(A) Improve the intensity of the clinical and fundamental research

(B) National & international networking and collaboration on therapy and patient management

(C) Clinical Trials

WORKING GROUP 6B

National & international networking and collaboration on therapy and patient management

President

Cassiman Jean-Jacques, Prof. dr. emeritus

Co-president

Eyskens François, diensthoofd Provinciaal Centrum voor Opsporing van Metabole Aandoeningen Antwerpen – kliniekhoofd Pediatrie UZA

Members

- Calcoen Piet, DKV
- Dahan Karin, Centre de Génétique humaine, Institut de Pathologie et de Génétique, Gosselies
- De Meirleir Linda, researcher Faculteit Geneeskunde en Farmaceutische Wetenschappen – Centrum voor Metabole Aandoeningen VUB
- Dooms Marc, apotheker UZ Leuven Campus Gasthuisberg – Belgische Vereniging van Ziekenhuisapothekers
- Gerits Pol, adjunct van de Directeur-generaal Organisatie Gezondheidsvoorzieningen, FOD Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu
- Hallet-Tordeurs Viviane, présidente de l'Association belge francophone de la rétinopathie d'origine génétique Retina Pigmentosa
- Haucotte Geneviève, secrétaire du Comité scientifique des Maladies chroniques et Affections spécifiques, INAMI
- Jageneau Ingrid, administratrice RaDiOrg.be
- Leroy Bart, Centrum Medische Genetica UZ Gent
- Loeys Bart, Centrum Medische Genetica UZ Gent
- Mortier Geert, hoofd Departement Medische Genetica Universiteit Antwerpen
- Revencu Nicole, centre de génétique médicale UCL
- Sokal Etienne, Cliniques universitaires Saint-Luc, Unité de gastroentérologie et hépatologie pédiatrique
- Stephenne Xavier, Cliniques universitaires St Luc, Unité de gastroentérologie et hépatologie pédiatrique, UCL
- Swinnen Elfriede, wetenschappelijk medewerker Centrum Menselijke Erfelijkheid KULeuven – Orphanet Belgium
- Verellen-Dumoulin Christine, directeur de l'Institut de Pathologie Génétique Gosselies
- Vikkula Miikka, de Duve Institute, ICP, UCL

WORKING GROUP 6C:

Clinical Trials

President

Musch Greet, directeur-generaal DG PRE FAGG

Members

- Delcroix Marion, kliniekhoofd Interne geneeskunde Pneumologie, UZ Leuven
- Eyskens François, diensthoofd Provinciaal Centrum voor Opsporing van Metabole Aandoeningen Antwerpen – kliniekhoofd pediatrie UZA

- Gobert Marjorie, legal counsel en bedrijfsjurist, Pharma.be
- Lhoir André, représentant de l'AFMPS et membre belge du COMP (EMIA)
- Revencu Nicole, centre de génétique médicale UCL
- Rogiers Ann, senior clinical assessor, FAGG
- Sokal Etienne, Cliniques universitaires Saint-Luc, Unité de gastroentérologie et hépatologie pédiatrique

WORKPACKAGE 7:
Training and education of health professionals

WORKING GROUP
Voorzitter
Poppe Bruce, Centrum Medische Genetica UZ Gent
Leden
- Aubry Chris, coördinator Vaardigheidscentrum, Faculteit Geneeskunde, KULeuven – bestuurslid RaDiOrg.be
- Belachew Shibeshih, Département des Sciences cliniques, Neurologie, Université de Liège
- Blaumeiser Bettina, Department of Medical Genetics UA
- Cogan Elie, chef du Service de médecine interne de l'Hôpital Erasme
- Devriendt Koenraad, Departement Menselijke Erfelijkheid, KULeuven
- Sznajer Yves, Centre de génétique humaine, UCL

The Fund Rare Diseases and Orphan Drugs

For more information:
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The Fund Rare Diseases and Orphan Drugs arose from the Steering Group for Rare Diseases and Orphan Drugs, which organised the first Belgian symposium on orphan drugs in the Parliament in 2006. The Fund is managed by the King Baudouin Foundation. It brings together all stakeholders in Belgium and endeavours to promote a coherent, consistent policy to enhance the quality of life of patients affected by a rare disease and those around them.

The Fund aims to take a structural, integrated approach to rare diseases, focusing on diagnosis and seamless care, and on research into and the development of appropriate medicines and treatments.

King Baudouin Foundation

Working together for a better society

www.kbs-frb.be

The King Baudouin Foundation is an independent and pluralistic foundation whose aim is to serve society. Our objective is to make a lasting contribution to justice, democracy and respect for diversity. Each year, the Foundation provides financial support for some 1,500 organizations and individuals committed to building a better society. Our activity domains for the coming years are poverty & social justice, democracy in Belgium, democracy in the Balkans, heritage, philanthropy, health, leadership, local engagement, migration, development, partnership or exceptional support for projects. The Foundation was created in 1976, to mark the 25th anniversary of King Baudouin's reign.

In 2011 we operate with a starting budget of 30 million euros. As well as our own capital and the large donation we receive from the National Lottery, we manage Funds created by private individuals, associations and businesses. The King Baudouin Foundation also receives donations and bequests.

The King Baudouin Foundation's Board of Governors draws up broad lines of action and oversees the transparency of our management. Some 50 colleagues are responsible for implementing our actions. The Foundation operates out of Brussels, but we are active at Belgian, European and international level. In Belgium, we have projects at local, regional and federal level.

We combine various working methods to achieve our objectives. We support third-party projects, launch our own activities, provide a forum for debate and reflection, and foster philanthropy. The results of our projects are disseminated through a range of communication channels. The King Baudouin Foundation works with public services, associations, NGOs, research centres, businesses and other foundations. We have a strategic partnership with the European Policy Centre, a Brussels-based think tank.

Outside Belgium, the Foundation is particularly active in the Balkans in projects that promote EU integration, tackle human trafficking and defend minority rights. In Africa, we focus on projects involved in the fight against AIDS/HIV and in promoting local development. The King Baudouin Foundation is also a benchmark in international philanthropy thanks to, among others, the international Funds that we manage, the King Baudouin Foundation United States, and our role in the Transnational Giving Europe network.

You can find further information about our projects, events and publications on www.kbs-frb.be. An electronic e-mail is also available if you would like to keep up to date with our activities. Please address any questions you may have to us at info@kbs-frb.be or call us on +32 (0)70-233 728.

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