Personal Reflections of a Patient Representative in an Appraisal Committee

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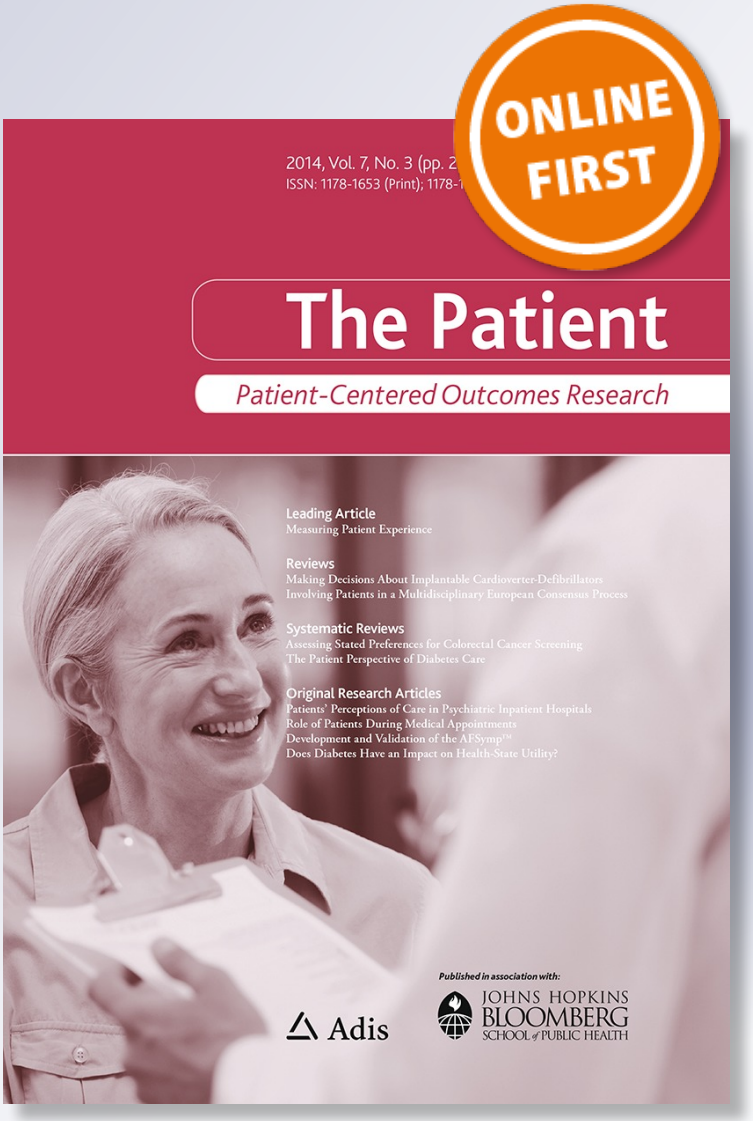

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COMMENTARY

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1 Introduction

In the summer of 2012, a large public debate took place in The Netherlands on the reimbursement of two expensive orphan drugs for Pompe and Fabry disease. On September 21, 2012 the appraisal committee (ACP) of the National Health Care Institute Package (ZIN) had to take a decision on this issue. Since its installation in 2008, I have been a member of the ACP as the patient representative. In this article, I will first outline the main discussions in the ACP of the scientific assessment and the societal appraisal process. Secondly, I will add some learning points for the international patient community. The overall message is that, right from the start, patient groups should be involved in all stages of decision making concerning both registration and reimbursement. This would make decisions more appropriate for patients, for the general public and for the healthcare system. Concerning rare diseases, the importance of a single European reimbursement procedure is discussed.

2 The Dutch Health Insurance System

In the Netherlands, the health insurance companies negotiate with healthcare providers on prices and volumes of cure and care. This follows a major overhaul of healthcare financing in 2006, from what can best be described as a socialised healthcare system to a regulated market with managed competition. The healthcare professionals decide whether someone is eligible for a particular treatment or diagnostic procedure, but they should use the agreed guidelines to reach their decision. Costs are reimbursed by the health insurance companies only when products are designated in what is called the insurance basic package or when special agreements between the insurance company and the healthcare provider exist. Health insurance companies have to accept all Dutch citizens for the basic package, but they can compete with each other on the price for this basic package.

2.1 The Insurance Basic Package

The content of the insurance basic package is determined by the Ministry of Health after previous advice from the National Health Care Institute Package (*Zorginstituut Nederland*, ZIN). As of April 1, 2014, ZIN has replaced the Health Care Insurance Board (CvZ). This organisation is engaged in the implementation of two Dutch statutory health insurance schemes: the Health Insurance Act (*Zorgverzekeringswet*, Zvw) and the Exceptional Medical Expenses Act (*Algemene Wet Bijzondere Ziektekosten*, AWBZ). ZIN gives advice to the Ministry of Health (VWS) regarding the insurance basic package including which drugs will be reimbursed [1]. ZIN uses the following four main package criteria:

- Necessity: Does the illness or the required care—given its context in society—justify societal expenses?
- Effectiveness: Does the care-form deliver what is to be expected?

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– Cost effectiveness: Does the care-form have an acceptable costs/benefits ratio?
– Feasibility: Is inclusion in the package feasible, now and in the long term?

Two committees with external experts, the Scientific Advisory Committee (WAR) and the Insured Package Advisory Committee (ACP), support ZIN (see Fig. 1).

The WAR assesses the scientific evidence on drugs and treatment methods that are candidates for the basic insurance package. The meetings of the WAR are not open to the public. After the WAR has done its assessment, the ACP discusses the relevant societal aspects of the drug or treatment. Meetings of the ACP are open to the public. The ACP's opinion is communicated to the Board of ZIN who uses this input to finalise their advice to the Minister of Health.

2.2 The ACP

Established in 2008, the ACP consists of nine members. Six are appointed by the Ministry of Health and they represent different disciplines. There is an ethicist, a politician, a surgeon, a health technology assessment (HTA) expert, an expert on the care of the elderly, and a patient representative. The three other members are the three board members of ZIN, one of whom chairs the ACP.

The ambition of the ACP was to run the basic insurance package as a 'bookcase', that is, a new drug or treatment should replace an older and less efficient treatment, while the overall budget remains more or less the same. However, it became clear that adding drugs or treatments was easier than discarding ones.

Moreover, external factors had an increasing influence on the original ACP concept. The introduction of the new health insurance system in 2006 had shifted the focus to market forces which led to a strong growth in the supply of health care which in the eyes of many was not at all necessary care. The subsequent economic recession led to austerity measures that also affected the healthcare budget. This led to the growing importance of the cost-effectiveness criterion and HTA reasoning in decision making. The Ministry of Health—in close cooperation with healthcare providers and healthcare insurance companies—arranged mutual agreements on the composition of the basic insurance package without consulting the ACP, or involving the ACP in a final phase only.

2.3 ZIN's Consultation Process and Patients' Organizations

ZIN consults with various stakeholders, including patients' organizations, before an advice is prepared. Recently the involvement of patients' organisations in the consultation process has been evaluated [2, 3]. The patients' organisations came up with a list of topics that should receive more attention in the advisory process. The main topics are shown in Table 1.

Experiences of patients' organizations with regard to the consultation process are mixed. They appreciate the consultation procedure as carried out by ZIN, but they frequently felt unsatisfied because of a perceived lack of

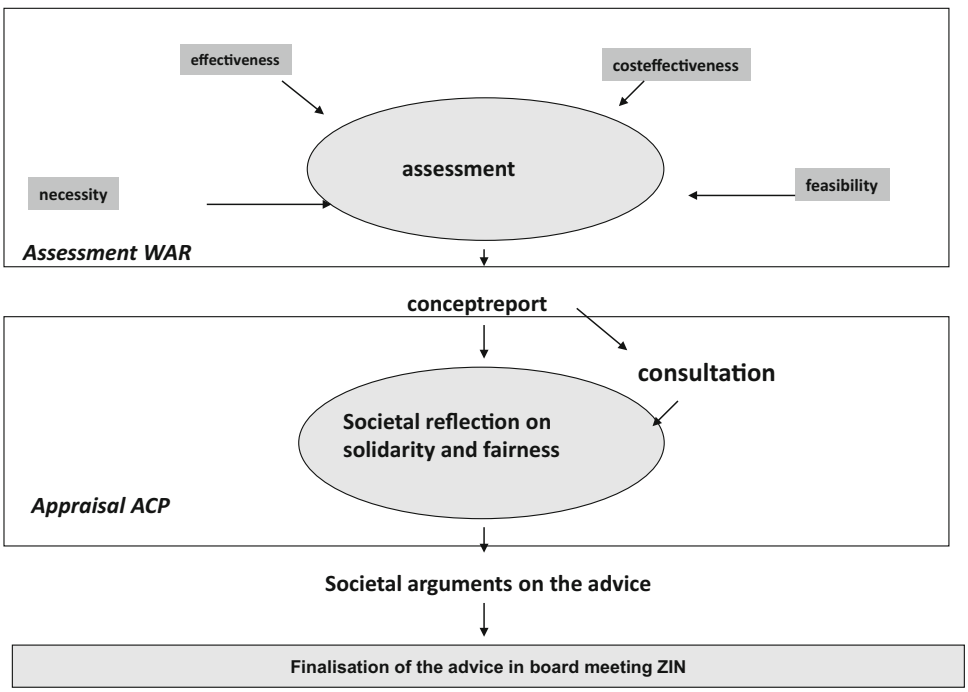

Fig. 1 Assessment and appraisal process, as installed at the National Health Care Institute Package (*Zorginstituut Nederland,* ZIN). *ACP* the Insured Package Advisory Committee, *WAR* Scientific Advisory Committee

Table 1 Topics to be covered by patients' organisations

1. Drawing attention to specific scientific evidence that was ignored before
2. Arguing for the importance of allowing off-label use of drugs in specific circumstances
3. Arguing that for some patients, a specific treatment may be a last resort
4. Arguing for the vulnerability of specific patient groups
5. Pointing to the limitations of producing scientific evidence, especially in the case of rare conditions
6. Pointing to the seriousness of the condition
7. Challenging expected savings of discontinuation of reimbursement, anticipating changes in behaviour on the part of patients and healthcare providers that may actually increase costs
8. Challenging the definition of medical care (domain discussion)
9. Challenging the scientific evidence when it does not concur with experiences of individual patients and healthcare providers

impact of their input. Often there is insufficient time to prepare a rigorous response. They felt that there was little opportunity for deliberation, and they would prefer to be consulted at a much earlier stage. They particularly felt they had very little influence on how a question is framed: what are the options, what are relevant outcomes, and what may be considered relevant evidence? Engaging them at an earlier stage of the assessment would, in their opinion, improve the opportunity for addressing basic questions. They were of the opinion that often the principles of evidence-based medicine were applied too strictly and that the limitations of this approach were not sufficiently acknowledged.

2.4 The ACP Discussion on Pompe and Fabry Disease

Certainly, the most striking discussion in the history of the Dutch Appraisal Committee ACP was the debate on the reimbursement of new drugs for two rare diseases, Pompe and Fabry disease, in the summer of 2012. The contributions of patients' organisations and healthcare providers in this case resulted in a substantial shift in ZIN's recommendations.

ZIN had concluded that, although medication for Fabry disease has some beneficial effects, it was too expensive relative to its benefits. They recommended to only reimburse the drug for Pompe disease for the small group of patients with the classic form of the disease. For 2 months this advice was in the centre of an intense societal and sometimes emotional debate in the media. The ACP meeting on September 21, 2012 was attended by over 200 visitors and had direct television coverage. There were contributions from physicians, pharmaceutical companies and impressive testimonials from patients with Pompe and Fabry disease.

Yann le Cam, executive director of the European Organization for Rare Disorders (Eurordis) analysed the gaps between EU centralised regulatory procedures and national HTAs or pricing and reimbursement decisions and made a strong and urgent plea to deal with this type of reimbursement procedure on a European level. This was also addressed by the treating physicians. They stressed the need for more data and unified patient registers on an international scale.

A key argument from patients' organisations and clinicians was that there is substantial heterogeneity among patients: some patients do not seem to respond, while others do. In the case of Pompe disease, which is a progressive disease, albeit slowly in some patients, stabilisation is already a major improvement, enabling patients to work and to live a sometimes normal life, even though some of them are already wheelchair bound. Moreover, the more personal outcome measures of patients and parents differed from the 'hard' outcome measures of HTA, especially the 6-minute walking test.

The ACP, and later ZIN as well, acknowledged the argument that—given the severity of the patients' condition—it was unethical to withhold them the medication. They recommended the Ministry of Health to take specific measures to ensure the continuation of the treatment. They suggested additional measures, such as an earmarked fund and a central indication committee, as well as to join forces with other countries to merge data and to negotiate with the manufacturers on the price of the drug. At the end of 2013, the Minister of Health decided to prolong the reimbursement of treatment costs for Pompe and Fabry disease within the basic insurance package for another 2 and 3 years, respectively, to enable improved data collection on the effectiveness of the treatment [4]. With the producers of the drugs, the Ministry negotiated a special price arrangement, which has not been made public.

3 Lessons Learned

3.1 The Structure

What main conclusions can be drawn from the decision to discontinue and then reinstate the reimbursement of the

treatment for Pompe and Fabry disease? It shows the lack of a coherent structure within ZIN to allow such a debate in an early stage. There is no possibility to merge the 'hard' criteria of HTA assessments with the more 'soft' considerations of moral factors such as ethics, equity, society views, etc. If, for instance, the scientific assessment of the WAR had included an open discussion with stakeholders, problems in the data (few patients, data collected from heterogeneous registers) and relevant patient reported outcome measures would have been identified early in the process. In this case, all these aspects converged in a public ACP meeting, quite some time after the original WAR assessment had been made. It also caused considerable damage to the public image of ZIN. Yet, at present, the ZIN procedures and the division of tasks between WAR and ACP are still the same. Little has been learned from this case.

3.2 Discontinuation of Treatment

A topic that has not been discussed previously within ZIN is the consequences of treatment discontinuation because of unfavourable cost-effectiveness ratios or QALYs. Discontinuation of treatment will lead to a gradual decrease in the health of patients with Pompe disease. In the long run they will need continuous breathing assistance and an earlier death will follow. Discontinuation of treatment therefore also creates substantial costs. A comparison of costs of treatment with a new but expensive drug with other necessary care when no drug is given was not discussed in the WAR but came up in the public debate as well as in the public ACP hearing. The topic resembles the discussion on the continuation of a drug after participation in a clinical trial. There is no final decision yet, the decision has been postponed for another 2 and 3 years, which still worries patients and families involved.

3.3 Access to Orphan Drugs

A third learning point is how to deal with development of and access to orphan drugs in general. On the one hand, research on rare diseases and the development of orphan drugs for serious, life-threatening unmet medical needs is stimulated, for instance, with the Orphan Drug Act (1983) in the USA and similar legislation in 1999 in the European Union [5]. On the other hand, however, there is no clear policy on how to grant access to the orphan drugs within the framework of the current reimbursement procedures. This disconnect can lead to a considerable waste in terms of research and development costs that cannot be earned back. Another question is whether the initial policy of ZIN to stop reimbursement of the treatment costs for Pompe and Fabry is in conflict with the Universal Health Care and the Right to Health concepts, as espoused in various international documents and conventions.

3.4 Pricing

The high development costs of orphan drugs and the risk of them not being reimbursed by insurance policies raises a fourth learning point. What is a realistic price for a particular orphan drug that allows industry to earn back its investments in the new drug? This needs further clarification in the future.

4 Recommendations for Stakeholders, Especially the International Patient Community

4.1 Consultation

The first recommendation is that patient groups should understand the importance of timely consultation. With orphan drugs and clinical trials already in the embryonic stage of development, they have to act and they should prepare themselves for this task. The same can be said about registration and reimbursement. For rare diseases, it is no longer acceptable to deal with these reimbursement procedures at the national level. The European Medicine Agency already has a good and long track record on timely patient and consumer involvement. But in my opinion organisations like EUnetHTA, national medicine agencies as well as the numerous ethics committees in Europe are lagging behind on patient and citizen involvement. Important contributions in meaningful patient involvement on registration and reimbursement procedures have recently been formulated by Eurordis, the Patient Charter from the UK Genetic Alliance, the EU funded Asterix-project and by Sharon Terry and Jayson Swanson in the United States [6–9].

4.2 Outcome Measures

There are some good examples of the development of new outcome measures by patient experts. For a long time, 'pain' was the most important outcome measure in research of arthritis. EULAR, the European League Against Rheumatism, which is a group of patient experts participating in scientific congresses on arthritis and rheumatism, has extended this outcome measure by the formulation of 'fatigue' and 'sleep disturbances' [10]. Another good example is the production of a number of short films in which young patients with Duchenne disease tell and show which outcome measures are relevant for them in daily life, like being able to comb their hair, raise a cup to drink or work on a laptop. These films have been presented at a

meeting of EMA where relevant outcome measures for potential new Duchenne drugs were discussed [11].

4.3 Funding

The next recommendation is on funding of patient groups. Compared with other stakeholders, the patient community often lacks sufficient resources to be fully equipped to play a serious role in these time-consuming and often complex consultation procedures. The European Commission or the EU member states have no clear vision on how patient groups should fulfil their 'third party' role in health care. This funding issue should be resolved in the near future in a joint process of patient groups with other stakeholders, the European Commission and EU member states [12, 13].

Such a process should also end discussions on possible 'conflicts of interest' of patient groups or patient representatives as they are funded by the pharma sector, governments or public–private partnerships. When one expects from patient groups that they play their own and independent role in health care, then it should be a logical consequence that they can act together with other stakeholders in public–private partnerships, like, for instance, the innovative medicine initiative (IMI).

4.4 Education

A fourth recommendation is education. Stakeholders should learn from each other about good practices in active patient participation in research as well as at the policy level. EU patient groups empower their membership through projects like value+, patient partner and recently the European Patient Academy (EUPATI). Other stakeholders could learn from these initiatives and actively encourage patient participation at an early stage in their activities [14–17].

4.5 Price

A final recommendation concerns the estimation of a realistic price for orphan drugs and the expected flood of personalised medications and diagnostics. It is not only necessary to have a better insight in the pricing process, but the underlying components should be carefully considered as well. It is my personal opinion that the massive burden of legislation—and sometimes also conflicting legislation—before introducing new treatment methods and drugs on the market, can be substantially reduced without compromising safety and at the same time lowering development costs. Risk–benefit scenarios should be revised against the background of whether or not alternative therapies are available. First steps have been taken by the UK Genetic Alliance [18].

5 Conclusion

In retrospect, my participation in the Appraisal Committee (ACP) of the Dutch Health Care Institute (ZiN) has been a positive experience and a learning period as well. It certainly added a wealth of new expertise to my position as 'patient expert' (in the EU) or 'patient advocate' (in the USA). I am convinced that it is not an example of 'tokenism' to have a patient expert in this appraisal committee. I absolutely had the impression that my input was not only heard, but also valued and used. Patient groups had to go through a learning process to get used to the stakeholder process of ZIN, but they learned quickly and sometimes could turn around decisions, as the example of Pompe and Fabry shows. Other important learning points were the perception of the growing distance between the 'hard' HTA evaluation measures and the 'more soft' outcome measures of patients and their families. The necessity of early involvement of patient groups in registration and reimbursement procedures, ideally at the EU level, has been discussed.

Finally, it can be argued that my personal situation, as a user of expensive drugs for my hemophilia, made me a 'biased' person within the ACP to judge the situation of patients with Pompe and Fabry's disease. I disclosed this 'potential conflict of interest' issue at the time I was asked to become a member of the ACP. At that time, and also later, this was not perceived as a problem.

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