

Patient empowerment and access to medicines: Insights from a scientist-patient suffering from erythropoietic protoporphyria

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Abstract

Patient representation during the evaluation of medicines by key decision makers such as regulatory agencies, Health Technology Assessment bodies, and healthcare payers is increasingly considered to add value to the appraisals and empowers patients, which means that they gain a more powerful voice over decisions and actions affecting their own health. As I myself suffer from the ultra-rare condition erythropoietic protoporphyria (EPP), I have participated as a patient expert in several discussions on access to afamelanotide, which currently is the only treatment for EPP and was approved in the European Union (EU) in 2014. As a molecular biologist with a PhD in EPP research, I consider myself having the necessary requirements to meaningfully contribute to such assessments. In this article, I share my personal experiences with regard to the discussions on access in Germany and England at the respective national competent authorities, the Federal Joint Committee, and the National Institute for Health and Care Excellence, respectively. In addition, I discuss the insights of the International Porphyria Patient Network, a group of highly empowered EPP patients effectively supporting national patient communities in their efforts to enable access to the afamelanotide treatment in their countries.

Keywords

Rare disease, orphan drugs, clinical trials, ethics, policy

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Personal empowerment

According to the World Health Organization's health promotion glossary, "empowerment is a process through which people gain greater control over decisions and actions affecting their health."¹

The essential first step before someone can even begin to gain control over one's own health is to know what one is suffering from. My parents and I searched throughout my entire childhood for an explanation of why I frequently had unbearable burning pain after spending even short periods of time outdoors on a sunny day. This pain was incapacitating and often left me in agony for days, during which I was unable to go to school, to sleep, to tolerate even weak light exposure, or the body heat of my parents

as they tried to comfort me. Not a single pain killer provided any relief, and the only option for me was to wait alone in a darkened and cooled room until the pain subsided. Of course, we tried everything that physicians recommended; still, not even high sun protection factor sunscreens helped prevent the symptoms despite the fact that they were obviously caused by sunlight. It must have been hard for my parents to see me in such a painful state

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without being able to alleviate or prevent it. What's more, the worst thing was that classmates, teachers, and even physicians did not believe me when I told them about the symptoms; I even brought photographs showing myself with swollen and burnt hands and face. Yet, this didn't stop some from making fun of me when I wore long clothing, hats, or used an umbrella on sunny days to protect myself from the sun's rays. Eventually, after I was sent to see a psychologist for my "made-up symptoms," I could no longer tolerate the derision and being treated with such condescension, and decided to stop sharing my experiences with healthcare professionals altogether.²

Finally, a full 26 years after the first symptoms, Dr Google provided the answer! In April 2006, I found myself yet again unable to sleep because, despite all precautionary measures taken, I had burnt myself in the strong sunlight of spring. I entered the combination of my symptoms in the Google search mask and, surprisingly, there was a new link in Wikipedia with an expression I had not encountered before "Erythropoietic Protoporphyrin." The short article was written by a young woman affected by erythropoietic protoporphyria (EPP) herself a few days earlier and it made my heart leap! That was the moment I obtained a name and an explanation for my symptoms, the moment I was all of a sudden no longer alone with this strange condition but part of a patient community with access to information and contacts to disease experts. It was the moment when everything changed.

Being a student in molecular biology, I of course instantly downloaded all the publications I could get my hands on. I was fascinated by the condition's pathophysiology and the unusual pattern of inheritance—which is neither dominant nor recessive, but dependent on an additional genetic variant that modulates the gene expression.³ Furthermore, I learned that in EPP, the biosynthesis of the red blood dye heme is affected and mutations in some of the genes of the pathway lead to accumulation of the precursor "protoporphyrin." And, with that, it also became clear why sunscreens never helped: protoporphyrin absorbs the energy of visible light, which then triggers the so-called "phototoxic reactions," burn-like injuries of the blood vessels and the surrounding tissue. Ultraviolet (UV) filters cannot prevent visible light from penetrating the skin and causing massive damage to the blood vessels. With the diagnosis, confirmed by a dermatologist after insisting to test me for EPP, I also had to accept that EPP is a lifelong, inherited condition associated with a higher rate of fatal liver failure. In addition, I learned that no therapy yet existed to prevent the painful phototoxic reactions; and, that because only one person in 150,000 is affected by EPP, this meant that the chance that a therapy would ever be developed was remote at best.⁴

A few weeks after I found the Wikipedia article, the German patient organization invited me to explain how I obtained my diagnosis at a small symposium held in

Darmstadt, Germany.⁵ There, I had the chance to meet many of the European EPP experts in person. Shortly thereafter, I was offered a PhD position by Professor Elisabeth Minder, the renowned expert physician and at that time Head of the Swiss Porphyria Reference Centre in Zurich, Switzerland. In 2007, I joined her team with the task to investigate gene expression patterns in EPP.^{6,7} Today, I am Head of the Clinical Chemistry laboratory in the Swiss Porphyria Reference Centre and responsible for the biochemical and genetic diagnostics of EPP and related heme biosynthesis defects, collectively called the porphyrias. In a team of committed research associates and university partners, I am actively contributing to a better understanding of these unique and under-explored diseases. When I joined the field, I could not have anticipated just how important the knowledge I would acquire would be.

The first effective treatment for EPP

A few months before I began to work in her laboratory, Professor Minder had started a small phase II clinical trial with five Swiss EPP patients testing an active compound, called afamelanotide, for the first time as a potential therapeutic approach to address EPP. The trial was triggered by a suggestion from Dr Rocco Falchetto, biochemist and Swiss EPP patient, who had the idea that enhanced pigmentation of the skin might act as a filter and prevent visible light from penetrating the skin and reaching the blood vessels. Afamelanotide is an analogue of the endogenous alpha-melanocyte-stimulating hormone (alpha-MSH) which induces melanin production in the skin. In addition, afamelanotide systemically activates strong anti-inflammatory and antioxidative cellular defense systems, both of which we now believe may be of greater relevance than pigmentation in preventing and reducing the severity of phototoxic reactions.⁸ All trial participants, Dr Falchetto being one of them, reported overwhelming clinical benefits and a substantial increase in the time they could spend outdoors and expose themselves to sunlight without developing phototoxic reactions—an effect they had never experienced with any previous treatment attempts.⁹

This first proof-of-concept study was followed by a larger, international phase 2 and an additional three multicentre randomized controlled phase 3 clinical trials, collectively including 347 EPP patients. All showed positive outcomes in their respective endpoints; EPP patients under treatment significantly increased the time they spent in direct sunlight without experiencing any pain and had less frequent and less severe phototoxic reactions.¹⁰ In 2008, the European Medicines Agency (EMA) granted orphan drug status for afamelanotide and, in 2009, through a special access scheme Italy made it available as a treatment for adult EPP patients. EPP patients in Switzerland had already benefited from access to the therapy for a period of 4 years through a compassionate use program and, from 2012, also

had access through a special access scheme enabling reimbursement for the treatment. The Italian and Swiss expert physicians later compiled the data from their 115 EPP patients receiving afamelanotide over the 8-year period in compassionate use and special access schemes, real-world evidence that demonstrated the good long-term safety profile, the pronounced and sustained increase in quality of life, and a treatment adherence rate of over 94%.¹¹

Having moved to Switzerland, I from 2012 on had the chance to test the afamelanotide treatment myself. Since a few minutes of exposure to sunlight can be sufficient to incapacitate me for days, I was naturally very cautious in the beginning and started with small steps like walking on the sunny side of the street or sitting on an “unsafe” seat in the bus that I knew would expose me to sunlight. Soon, I became more daring and attempted slightly riskier experiences—and made the same life-changing experiences as the other EPP patients I am in contact with. Today, under treatment, I am able to fully function in daily life: I can do my job in diagnostics, teach at the university, although the course is held in May and I have to travel to the other side of the city, and I can join social activities outdoors with friends and colleagues—sometimes I even find myself completely forgetting that I have EPP at all!

Approval of afamelanotide: let the sunshine in!

In the beginning of 2012, the approval process for afamelanotide at the EMA started. Given the overwhelming evidence for safety and effectiveness, the patients and disease experts anticipated a timely approval and subsequent rapid access to the afamelanotide treatment. However, during the proceedings, the EMA rapporteurs unexpectedly questioned the extent of the benefits as well as whether the treatment effects would be meaningful to patients.¹² Because the rapporteurs’ assessment was in absolute disagreement with our own life-changing experiences of the therapy, Dr Falchetto and I gathered the international EPP patient community, engaged in discussions with EMA officials and requested to be included in the process: nothing about us without us!

After an extensive exchange with the regulatory body, in April 2014 six EPP patients and carers, along with several EPP disease experts, were finally invited to an ad hoc Special Advisory Group meeting with EMA representatives to provide firsthand insights on the impact EPP has on affected individuals and their families; more importantly, they provided direct testimony as to the life-changing effects of the afamelanotide treatment. As I had been perplexed by the persistent perception that the afamelanotide treatment provided limited benefits, after the meeting I thoroughly investigated the documents on the assessment: in the pivotal study published in the *New England Journal of Medicine*,¹⁰ patients under treatment

exposed themselves for an additional 28.6 h to direct sunlight without experiencing any painful phototoxic reactions compared to the untreated control group. In the EMA documents, this outcome was reduced to 24 h in direct sunlight by a post hoc calculation requested by the rapporteurs and called Hodges–Lehmann shift estimator, which is an unusual way to calculate the median. Furthermore, the remaining time in sunlight was divided through the entire trial period of 180 days and subsequently reported as a benefit of 8 min per day only—without taking into account that the trial period obviously comprised, for example, rainy days during which no sun exposure was possible, and that the trial participants were also limited in their outdoor activities by working hours and other indoor duties. In my opinion, the effectiveness of any therapy needs to be assessed under the circumstances that actually apply and matter to the patients. For us EPP patients, it is of paramount importance that under treatment, we are able to expose ourselves to light for a prolonged period of time if necessary. Hence, using an average outcome to calculate effectiveness makes little sense.

In September 2014, the EMA took a significant step towards more patient inclusion in their processes and for the first time in their history involved patients in a full regulatory meeting with the Committee for Medicinal Products for Human Use (CHMP) to discuss the benefits and risks of the afamelanotide treatment. On that occasion, I was granted the opportunity to explain to the entire CHMP how EPP had impacted me and how the treatment changed my life and that of my fellow patients. In October 2014, the EMA recommended afamelanotide for approval under exceptional circumstances for the prevention of phototoxicity in adult patients with EPP.¹³ While this was an undeniably positive outcome for EPP patients, significant challenges remained: although several patient representatives requested the adjustment of the potentially misleading recalculation of the trial results, the rapporteurs nonetheless included it in the most prominent chapter on the benefit–risk balance in their final European Public Assessment Report (EPAR) of afamelanotide.¹⁴

At that time, the recalculation of the trial results seemed to be a detail of limited importance to us and we could not have anticipated the issues we would face because of it: approval under exceptional circumstances is a type of marketing authorization that can be granted in case a condition is so rare that the treatment effects cannot be accurately quantified. For the afamelanotide treatment, the EMA stated that it would be, conceivable that the complexity of the EPP patients behaviour and the dependence of phototoxicity with environmental factors in real life differ to such an extent that the actual benefit cannot be captured in conventional clinical trial designs, for ex. [example, J.B.A.] randomised blinded clinical trial design and that no design could address this matter taking into account the current scientific and technical knowledge.¹⁵

In addition, in the EPAR the agency stressed the strong ethical imperative to treat EPP:

As EPP is connected with uniquely painful, disfiguring [sic], debilitating, socially disabling and in the long run potentially life-threatening phenotypic manifestations and no authorised medicinal products exists for EPP there is currently a clear unmet medical need for treatment of patients with EPP.¹⁶

(No) access to the only treatment

Afamelanotide was approved for the treatment of adult EPP patients in the European Union (EU) at the end of 2014. In April 2019, most EPP patients in Europe, however, still do not have access to the only treatment for their condition and are still unnecessarily suffering from frequent excruciating pain, social isolation, and impaired life choices. What went wrong? Before a newly approved medicine reaches patients, most European countries perform a Health Technology Assessment (HTA) to evaluate the benefits in relation to the costs of the new product in order to support decisions on whether it should be reimbursed by the respective national health systems. In my role as a patient and disease expert, I was directly involved in the HTA proceedings in Germany and England.

In Germany, the national competent authority is the G-BA (Gemeinsamer Bundesausschuss; Federal Joint Committee). In its early assessment report, the G-BA questioned the extent of the benefit of the afamelanotide treatment with a direct reference to the 8 min stated in the EMA document.¹⁷ Based on the assumed small effectiveness, the G-BA came to the conclusion that the additional benefit of the afamelanotide treatment is small, which would have made reimbursement by German health insurers very unlikely. Being the scientific advisor of the German patient organization at that time, I supported the patient representatives in their preparation for the appraisal proceedings. In addition, I had the opportunity to register as a disease expert and in that capacity was able to provide a written statement as well as participate at an oral hearing. Likewise, Professor Minder was asked to provide her inputs as a medical disease expert as well. The G-BA committee finally changed their assessment from “small benefit” to “not quantifiable,” which is in line with EMA’s approval under exceptional circumstances. Because the manufacturer and the representation of the German health insurers could not reach an agreement over the pricing of afamelanotide, an arbitration board was called to facilitate a pricing agreement which would balance the budget impact on the German health system against a reasonable return on investment for the manufacturer. After a pricing agreement was reached, the manufacturer of afamelanotide adopted a uniform approach using the German agreement as the basis for its pricing policy in other European countries. Since April 2017, afamelanotide is reimbursed

in Germany, and all adult EPP patients are entitled to access the treatment.

Given our experience in Germany that HTA bodies might not understand the true benefit of the afamelanotide treatment when they base their assessment on the EMA documents and that patient representatives might need to explain the results of the clinical studies on a scientific level, Dr Falchetto and I came away with a renewed sense of urgency to proactively strengthen international cooperation, and to these ends, in February 2016, we launched the International Porphyria Patient Network (IPPN).¹⁸ In Spring 2016, the scoping phase of the afamelanotide treatment at the National Institute for Health and Care Excellence (NICE) in England started. IPPN was admitted as a stakeholder and sent two British EPP patients as delegates to the scoping workshop and together with the national disease patient organization, the British Porphyria Association (BPA), provided feedback on the draft-scoping document. Thereafter, for unknown reasons, IPPN was excluded from subsequent proceedings; and only after an extensive exchange with NICE officials it was readmitted to the process; however, IPPN was not allowed to participate in the committee meetings and could only submit a written statement.

Similar to our experience with German bodies, the NICE committee also concluded that the afamelanotide treatment would only provide a “small benefit” and, based on this assessment, did not recommend reimbursement by the National Health Service (NHS) in their preliminary Final Evaluation Determination.¹⁹ EPP patients during the committee meetings shared their firsthand experiences with the afamelanotide treatment, which they described as being nothing less than life-changing, and stated that, under treatment, they were able to spend several hours outdoors on sunny days in contrast to the few minutes without the treatment. These testimonies were confirmed at the committee meetings by the expert physicians from the British Association of Dermatologists (BAD), by the written statement of IPPN and, in addition, by 34 online comments from national and international EPP patients and carers submitted during the consultation phase. In its submission, the IPPN further explained the recalculation of the original trial results by the EMA. The NICE committee in their documents of the proceedings commented that the patient and expert physicians input “was noted” and “has been considered.”²⁰ We were therefore rather surprised to learn that even after the second committee meeting, NICE maintained their negative recommendation and initial interpretation of a small benefit.

As part of the NICE appraisals, stakeholder groups have the possibility to file an appeal on one or all of the following grounds: in making the assessment that preceded the recommendation, (1) NICE has (a) failed to act fairly and (b) exceeded its powers or (2) the recommendation is unreasonable in the light of the evidence submitted to NICE. All stakeholders, that is, the IPPN, the BPA, the BAD as well as the manufacturer filed a written appeal

against several aspects of the assessment and in July 2018 attended the oral appeal hearing in London. IPPN was represented by a British EPP patient who participated in one of the clinical trials for afamelanotide, a barrister and myself. The independent appeal panel upheld six appeal points, three of which were provided by the IPPN, in each potential ground for appeal.²¹

The appeal panel concluded that NICE acted unfairly when they excluded the IPPN from the second committee meeting. All stakeholders at the appeal meeting reiterated that the IPPN contributes to the unique perspective of patients under long-term afamelanotide treatment. From early childhood on, EPP patients know that sunlight causes extremely painful phototoxic reactions, which cannot be managed by any known pain remedy. While the majority of EPP patients already notice some relief after a few weeks of treatment, like in the clinical trials, the full extent of the benefit is only known by those patients with long-term experience who show a near complete loss of anxiety to light exposure and who unlearn their light avoidance behavior. The appeal panel was also concerned “whether the methodology used in the evaluation discriminates against patients with EPP and if so what reasonable adjustments should be made.” And most importantly, the panel shared the view of the disease experts and patients that it was unreasonable given the evidence submitted to NICE to state “that the trial results show small benefits with afamelanotide.” As the assumed small benefit is the main reason given by NICE to not recommend afamelanotide for reimbursement, this decision of the appeal panel in our opinion should lead to a fundamental reassessment of the entire cost–benefit evaluation by the NICE committee.

As a direct result of the upheld appeal, a third committee meeting was held in March 2019, this time including IPPN, for which I was the representative. At the time of writing, we are waiting to hear back from NICE and hope that, with the appeal decision and the additional evidence submitted for the third meeting, British sufferers will soon gain access to the only existing treatment for their condition.

An international network of highly empowered patients to enable access to medicines

Dr Falchetto and I first met when I moved from Germany to Switzerland in 2007. After a while, we realized that we would build a fine team and started to work together in trying to understand the regulatory requirements of the approval and HTA proceedings. Over time, we came into contact with other porphyria and EPP patients and carers, many of whom have professional backgrounds in science or medicine, and all of whom share the same desire to raise awareness on their condition and on the porphyrias in general, and enable therapy access in their home countries, with the current focus being access to the afamelanotide

treatment. As a result, the IPPN has developed into a group of highly empowered patients whose goal it is to raise awareness on the severity and impact of porphyria on patient lives and for the issues of therapy access, and to engage in discussions with regulators, HTA bodies, health-care payers (e.g. health insurers or national healthcare services) and other stakeholder groups. In addition, we support national disease patients and organizations with the specific knowledge we have obtained during our activities around the afamelanotide access discussions. We can proudly state that the IPPN was directly or indirectly involved in most of the successful access discussions to afamelanotide that have taken place to date (Table 1).

Based on our experience with afamelanotide, we identify four critical success factors for the facilitation of therapy access:

- A strong national disease patient organization.
- Dedicated expert physicians engaged in the proceedings.
- Involvement of IPPN either directly as a stakeholder in the proceedings or indirectly supporting patient representatives and/or disease experts.
- HTA proceedings that enable meaningful patient and expert physician participation.

Meanwhile, many countries do have active patient organizations and disease experts who actively support their porphyria and EPP patients. The main issue in my opinion is whether meaningful participation in the proceedings is enabled by the HTA bodies.

Empowered patients in discussions on medicines access: meaningful participation

Patient empowerment in access discussions is only ensured if meaningful patient participation and representation is truly actualized and the insights provided by the patients are effectively considered for the evaluation:

1. First of all, involvement of patients living with the condition is the fundamental requirement for meaningful patient participation: in many countries, for example Sweden, only “proxy” patients who are usually not affected by the condition under evaluation but suffer from some other disease are involved in the HTA proceedings.²² Obviously, proxy patients cannot provide meaningful insights when specific disease characteristics and clinical effectiveness are being discussed—the most important aspects when judging the benefit of new treatments. Especially in orphan diseases, proxy “representation” is highly inappropriate, because the conditions are usually not known either to members of the assessment body nor to the proxy patients themselves.

Table 1. Countries with full or partial access to the afamelanotide treatment for EPP patients.

| Country | Decision on reimbursement | Access since (% of patients) | Contribution of IPPN medicines access group members |
|---------------|----------------------------|------------------------------|---|
| Switzerland* | na (special access scheme) | 2012 (100) | Discussions with health insurers, organization of a public awareness campaign |
| Netherlands** | Positive | 2016 (100) | Knowledge transfer to national disease patient representatives and expert physicians |
| Italy* | Positive (regional level) | 2009 (70) | Discussion with regulatory and HTA bodies, organization of a public awareness campaign |
| Germany* | Positive | 2017 (50) | Participation as disease expert during HTA proceedings, organization of a public awareness campaign |
| Austria* | na | 2017 (10) | Positive reimbursement decisions for individual cases, start of the public awareness campaign |
| Belgium | Ongoing | 2017 (5) | IPPN providing support to national patient organization |
| Wales | Negative | 2017 (0) | No IPPN involvement |
| Norway | Negative | 2018 (0) | No IPPN involvement |
| England* | Ongoing | (0) | IPPN is a stakeholder in the proceedings and the appeal process |
| Sweden** | Ongoing | (0) | Knowledge transfer to the national disease patient organization and expert physicians |

EPP: erythropoietic protoporphyria; HTA: Health Technology Assessment; IPPN: International Porphyrin Patient Network.

*Significant and direct contribution.

**Indirect support.

- When patients are included in an assessment, it is of utmost importance to include the groups most relevant to the evaluation. In the assessment of afamelanotide for the treatment of EPP, firsthand long-term experience is the most relevant insight shared by the patients. In most countries, EPP patients do not have access to treatment with afamelanotide; therefore, only organizations like the IPPN can provide this perspective, a reason shared by the NICE appeal panel, as detailed above.
- Patient input needs to be effectively considered; otherwise, patient involvement is reduced to an empty exercise in tokenism. In the appraisal of afamelanotide at NICE, the EPP patient representatives from the national patient organization at the committee meetings testified to the life-changing effects of the treatment and that, under therapy, they are able to live an almost normal life. "More time in sunlight for less pain" is not a surrogate marker of unknown significance but a clinically meaningful endpoint directly assessable by every EPP patient under treatment. Nonetheless, the NICE committee first essentially ignored the patient testimonies and rated the benefit of the treatment as "small," and it had to come to an appeal to revise this incorrect assessment.
- Involvement of highly empowered patients should not be a necessity to make their voices heard: having a group of highly empowered disease patients with experiences with previous approval and appraisal proceedings is highly exceptional for an ultra-rare condition and should not be a *conditio*

sine qua non for meaningful patient involvement in an appraisal proceeding. We are concerned that other disease groups without such representation might fall through the cracks of the system and be denied access to potentially life-saving and life-changing treatments.

- Meaningful patient involvement is only possible if a fair, consistent, and transparent HTA proceeding is ensured: while on one hand, it is good to have the possibility to appeal an appraisal of NICE, I find it rather alarming that a national body demonstrably failed to act fairly and made obviously unreasonable decisions in the first place. And while the appeal panel decided that the evaluation has to be revisited, it is nonetheless remitted back to the very same NICE committee responsible for the previous evaluation.

Conclusion

Our case is an example for the difference the input of highly empowered patients during access discussions can make. However, it is urgently necessary to improve appropriate inclusion of the patient perspective in order to ensure that decisions reflect outcomes that are relevant to the patients.

As patients and patient representatives, we are best placed to know if a therapy benefits us or not, and we should be given a weightier voice over decisions and actions affecting our lives. This is only possible if decision makers truly listen to our insights and treat us as equal partners when assessing new health technologies, particularly in the case of ultra-rare conditions with no alternative treatment options and lack of disease understanding.

Take Home Messages

Lessons learned—scientist-patient view on approval proceedings and value assessments of orphan drugs.

Erythropoietic protoporphyria (EPP) is one of the very few ultra-rare conditions for which a safe and effective therapy has been successfully developed. However, despite it being the only treatment for EPP, most patients in Europe still do not have access to afamelanotide, more than 4 years after its approval in 2014. Being a patient, I would like to see patient needs at the centre of all regulatory evaluations and value assessments:

1. Patients are directly affected by every decision concerning their treatment and, therefore, need to be included in all relevant steps during proceedings on national and international level.
2. Especially in rare diseases, patients and disease experts know the most about the conditions and can contribute unique insights. However, their inclusion is only meaningful if they are also accepted as equal stakeholders.
3. Patients with rare diseases have the same right to access to healthcare as patients with more common conditions. Especially in conditions connected with pain, a moral obligation exists to alleviate it if such a possibility exists. For EPP, the European Medicines Agency (EMA) determined that no further placebo controlled trials should be conducted, as it would be ethically not acceptable since patients in the control arm would be at risk of developing phototoxic reactions and severe pain.¹⁵ Therefore, denying access to the afamelanotide treatment after approval is ethically highly questionable.

Being also a scientist, I understand that regulatory agencies and national bodies are faced with challenges when assessing the eligibility of orphan drugs for approval and reimbursement, respectively. Nevertheless, several key aspects could be optimized in order to ensure a fair and more rational process.

4. Duplication of efforts between different official bodies should be avoided: after extended analysis, the EMA determined that the efficacy of the afamelanotide treatment cannot be accurately quantified because of the rarity and complexity of the condition, but that patients have a better quality of life under treatment and that the benefit of the treatment outweighs its risks.¹³ National Health Technology Assessment (HTA) and other reimbursement bodies should not try to replicate the regulatory scientific evaluation, but rather resort to the rational which led to regulatory approval, as a new assessment unnecessarily multiplies the efforts and severely delays access to the treatment.
5. Consistency in the scientific assessment needs to be ensured: on one hand, in their justification for approval, the EMA determined that the efficacy of the afamelanotide treatment cannot be accurately quantified.¹³ However, the EMA then also requested scientifically questionable post hoc analyses and determined that the extent of the benefit “appears small.”¹⁶ Obviously, an effect either can have a precise value or is not be quantifiable, but not both at the same time. We have repeatedly experienced how the contradictory representation of the EMA’s conclusions created confusion among the national bodies assessing the afamelanotide treatment for reimbursement and the EMA should revise their documents in order to avoid ambiguities.

When in 2014 I became a patient representative in the approval proceedings for afamelanotide at the EMA, I did not expect that we patients would have to fight so intensively for the points detailed above. It seemed obvious that patients and expert physicians would be included in the discussions on clinical benefit and effectiveness of a treatment, and that assessment reports of public authorities would be revised in view of inconsistencies or new evidence. Unfortunately, this was not the case and ours is only but one example of many which illustrates the issue with orphan drug approvals and value assessments. Therefore, on the back of this experience and in order to empower patients to contribute with a stronger voice to approval proceedings and value assessments of orphan drugs, I co-founded the International Porphyria Patient Network, a working group of patients with a professional background in science, medicine, and other relevant professions.¹⁸

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