European Haemophilia Consortium
Office of the National Member Organisations

EHC Stakeholders Round Table

Access to new therapies: opportunities, challenges and barriers

Meeting Report

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*The **19th EHC Stakeholder Round Table**, chaired by Radoslaw Kaczmarek, EHC Steering Committee member, addressed the issue of **Access to new therapies: opportunities, challenges and barriers**. It was a particularly timely discussion, as the EHC had just returned from an important meeting with the European Medicines Agency (EMA) on these issues.*

Speakers and participants addressed both the science behind novel longer-acting haemophilia products as well as the ways in which these products could revolutionise haemophilia care in Europe. At the same time, they addressed the regulatory barriers to timely, cost-effective and sustainable access that currently exist in Europe, and discussed the significant ramifications of such a delay in access.

Participants heard perspectives from patients, clinicians, industry and the EHC. Speakers included Brian O'Mahony, EHC President; Dr Paul Giangrande, Consultant Haematologist, Oxford University Hospitals NHS Trust; Dr Hartmut Landgrebe, Associate Director of Regulatory Affairs, CSL Behring; Dr Armin Reininger, Medical Doctor Bioscience Haemophilia, Baxter; Prof Karin Knobe, Vice-President Medical and Science Haemophilia, Novo Nordisk; and Dr Geoff McDonough, Chief Executive Officer, Sobi.

- **Welcome and Introduction – Radoslaw Kaczmarek, Chair and EHC Steering Committee Member**

Radoslaw Kaczmarek welcomed participants and speakers to the 19th EHC Round Table of Stakeholders.

He highlighted the timeliness of this topic as the EHC just completed a mission to the European Medicines Agency (EMA) in London to address the paediatric requirements for clinical trials, orphan drug designation and the dangers of market exclusivity.

He also underscored the importance of this topic to haemophilia patients throughout Europe and invited participants to engage in an active and fruitful discussion.

- **A Clinical Overview of New Haemophilia Products – Dr Paul Giangrande, Consultant Haematologist, Oxford University Hospitals NHS Trust**

New longer-acting FVIII and FIX products may provide opportunities to substantially increase trough levels and thereby dramatically improve the treatment and the overall quality of life of people with haemophilia, said Dr Paul Giangrande.

Opening his presentation, Dr Giangrande gave an overview of the products currently under development by the pharmaceutical industry. He outlined their promise, but also drew attention to some failures and other potential problems, for example the different types of assays required. In addition, he highlighted that the technology being used was exclusively recombinant, and said that the role of biosimilars should also be included in the conversation.

Dr Giangrande underscored the importance of longer-acting products, as a result of which haemophilia patients could be better protected against bleeds, children could have early prophylaxis, “on demand” treatment could be carried out with fewer doses, and patients with haemophilia undergoing surgery could benefit from better clinical management.

Citing the published views of Mark Skinner, former President of the World Federation of Hemophilia (WFH), Dr Giangrande said that higher trough levels are a necessity and only longer-acting products can help to achieve them in a cost-effective and sustainable manner. In his view the current FVIII trough level of 1% is “wholly insufficient” and the ideal level would be 15%. Aware of the prohibitive short-term costs, however, Dr Giangrande argued that an incremental improvement towards higher baseline levels of 3% or 5% should be the next step. “Improving patients’ quality of life should drive treatment decisions,” he said, “not economics.”

Citing the regulatory differences between the US Food and Drug Administration (FDA) and the EMA, he regretted that European patients would likely not have access to these products for several years after US patients.

Dr Giangrande also voiced his concerns over the possible “abuse” of orphan drug designation by the developer of the first longer-acting product to enter the market. He warned that such a scenario would create a “monopoly” that would “throttle competition” and ultimately be of significant detriment to haemophilia patients throughout Europe.

- **The Patient Perspective: Access to New Therapies – Radoslaw Kaczmarek, EHC Steering Committee Member**

Radoslaw Kaczmarek commented on the new era in haemophilia product development and innovation, and outlined how this might benefit patients throughout Europe.

He gave an overview of the research behind new haemophilia therapies including protein modifications to prolong half-life as well as alternative strategies to enhance haemostasis. He illustrated how, from a patient perspective, these advances in treatment represent the largest potential break-through since the invention of clotting factor concentrates.

The impact on patients' quality of life could be dramatic, he said. Longer-acting products would allow better management of bleeds, with most bleeds effectively treated with one infusion, and higher trough levels would make physiotherapy more effective.

Speaking from a personal capacity, Mr Kaczmarek told participants that he himself is currently participating in the clinical trial of a longer-acting FVIII product. Not only have the twice-weekly infusions allowed effective prevention of bleeds, he said, but they have also enabled him to resume an important resistance exercise regime after a three-year break.

Poland, a former Eastern Bloc country, still has a limited choice of haemophilia products and most of them are plasma-derived, he said. Longer-acting products could rapidly improve haemophilia care in countries such as his that have lagged behind their peers, he continued, drawing a parallel to Africa graduating from a telephone booth directly to a cell phone. But even without such leaps, these products could still benefit patients throughout Europe by reshaping the pricing landscape of currently available products, he said.

To do so, however, would depend on the cost. Mr Kaczmarek reminded participants that in Poland like in many other countries, cost is the main – if not the sole – criterion for tenders. "The new generation of products must be cost-effective to be accepted for funding by health authorities," he said.

- **The EHC Perspective: Access to New Therapies – Brian O'Mahony, President of the EHC**

There is big excitement about longer-acting products amongst the European patient community, Brian O'Mahony told participants, citing the prospect of fewer infusions for children, fewer

problems with venepuncture, the potential for individualised therapy, the possible changes to prophylaxis regimes or intervals and the possible changes to on-demand treatment.

The economic opportunities are exciting as well, Mr O'Mahony said. The new generation of products could transform not only haemophilia treatment but also the haemophilia market. The cost of recombinant products could decrease, thereby opening new markets, and potentially the cost of plasma-derived products could decrease as well.

However, this potential to be transformative will depend entirely on whether these products are introduced and available in Europe on a cost-effective basis. If not, European governments will not allow these products, he said, as HTAs are set to become the "normal reflex" in the future.

The fact that the first longer-acting product will be licensed and enter the US market first will be a challenge for Europe, which has lower average prices than the United States. "We will have to work incredibly hard to get these products through," Mr O'Mahony said, adding that pharmaceutical companies "will have to work with us to persuade governments by making the products available on a cost sustainable basis."

However, an even bigger challenge to the community would be the application of market exclusivity for the first product to hit the market. Some products may be better for some patients, he told participants. "We do not want to see just the first of these; this is not the Olympics and there should be no gold medal for the first one through the gate," he said.

Mr O'Mahony explained that orphan drug designation made sense for very rare diseases that only had one product on the market; but haemophilia has 17 plasma-derived and seven recombinant factor products in Europe.

"The EHC's position is that there are three distinct and different protein modification or enhancement approaches, and therefore there are three distinct and dissimilar products," he told participants. "As a community we welcome all options and approaches; we need many products; we need choices; and we need competition," he said.

As a result, Mr O'Mahony said he would be calling on pharmaceutical companies to forego their rights to market exclusivity, should their products be the first on the market. "We do not see this as a race to the finish with winner takes all," he said, "because that would damage haemophilia care in the future."

- **The Industry Perspective – Dr Hartmut Landgrebe, Associate Director of Regulatory Affairs, CSL Behring**

Dr Hartmut Landgrebe gave an overview of the mechanisms that come to play between patients/physicians, authorities and the market to lead to the successful introduction of new haemophilia products. "We stand in the middle between the science and the law," he said, "we are mediators."

Dr Landgrebe also spoke of a great learning curve that the pharmaceutical industry throughout the world had gone through, and underscored that both patients and physicians confirmed the safety and utility of clinical trials.

He then provided an update on the development status of CSL Behring's longer-acting products, and outlined the company's goals, objectives and long-term vision for these products, including that they might drive new standards for haemophilia care going forward.

- **The Industry Perspective – Dr Armin Reininger, Medical Director, Bioscience Haemophilia, Baxter**

"The future of haemophilia care should be tailored," said Dr Armin Reininger, who focused his presentation on the importance of individualised therapy and the need to consider different trough levels for patients with different lifestyles.

He also presented "haemophilia puzzle pieces," which include annual bleed rate zero, long-term joint health, quality of life, efficacy and safety, PK-driven prophylaxis doses, adherence, factor consumption, prophylaxis data and vision of bleed-free world.

"There are a lot of puzzle pieces and they are not well aligned yet," Dr Reininger said. He also warned that the latest product on the market might not necessarily be the right one for patients. "We need to be very careful with the transition," he said, "otherwise the ball may be dropped."

- **The Industry Perspective – Prof Karin Knobe, Vice-President, Medical and Science Haemophilia, Novo Nordisk**

The haemophilia community is entering an exciting period of innovation, said Prof Karin Knobe.

Representing the department in Novo Nordisk where clinical trials are designed, Prof Knobe gave participants an overview of the active haemophilia trials that Novo Nordisk had in 33 countries in 2012, not counting local trials. She also commented on the EMA clinical trials guidelines and emphasized the length of the process from inception until products reach the market.

- **The Industry Perspective – Dr Geoff McDonough, Chief Executive Officer, Sobi**

Dr Geoff McDonough described the "potentially enormous value in new therapies" but also underscored that patients are placing an equally "enormous value" on choice; "choice is fundamental," he said.

He argued that the EMA could and would be responsive to what patients want when deliberating the question of exclusivity. He also addressed his peers, commenting that industry has a "responsibility to show on day zero that anything we bring to the community will be sustainable over time," and asked them, "Can any of us answer that question?"

"If we are attentive and really listen to patients, in different countries, and in different stages of life," he said. "If we can include all the stakeholders to describe our rationale, if we can create a platform for evidence over time – with partnership – we can help."

- **Question and Answer – Radoslaw Kaczmarek, Chair and EHC Steering Committee Member**

Alain Weill, President of the WFH, launched the discussion by stating the WFH's support to the EHC. "The WFH is in full alignment with the EHC on this issue, and they have our total support and cooperation," he said, referring to the call for industry to waive its right to market exclusivity for these products.

Mr Weill then followed up with an open question to industry, asking what they will do when new therapies enter the market and patients switch products. “It’s a question about global equity and sustainability,” said Dr McDonough, adding that industry and patients should work in partnership. Mr Hansjörg Dürr from Bayer agreed. “It is not a capacity question,” he said, “it is a partnership question.”

Driving change will require new innovation, and that will require competition, said Mr Dürr. Price will also be a factor, said Dr Reininger, who explained that price and other aspects would be important to provide patients with options. Dr Mathias Juers from CSL Behring said that many scientific questions remained unresolved and that more data, more products and more time were needed.

The EHC is trying to ensure, with the EMA, that haemophilia patients don’t see their options removed, said Mr O’Mahony. But costs will remain the focus, added Dr Giangrande who warned, “There will be a yawning gap in price between new products and biosimilars.”

Unfortunately, the EMA cannot consider economics, said Mr O’Mahony, and underlined that the EHC would continue its “constructive engagement” with them. The EHC will also aim to be in the committee room as patient representatives when market authorization applications come forward. “It is the beginning of the process,” said Dr Giangrande. He and Mr Kaczmarek both underlined that “it will be crucial that all stakeholders and not only the EMA are sympathetic.”

Mr O’Mahony asked participants for their views on the EHC’s approach with the EMA. “The EHC is taking exactly the right approach,” said Mr Dürr, “we want patient advocacy on the table.” Prof Knobe agreed, saying that the EHC is doing all the right things and encouraging the EHC to continue working with the EMA to ensure patients have options and choices. “Choice will drive access,” she said, adding that orphan drug designation in the case of the haemophilia community should be treated differently than for other rare diseases.

Mr Dürr asked how a tender process would work in light of questions over choice. Mr O’Mahony said that this will be considered when the EHC does its 2013 European survey on tender processes. He added that the tender guidebook he authored for the WFH would be rewritten next year. “The problem,” he said, “is when patients and doctors are excluded.”

Participants also discussed long-term outcomes, safety options and data. Dr Giangrande underlined that the pharmacovigilance work of EUHASS would continue. Mr Jan Maarten ten Brundel from Baxter suggested that new criteria might be added to it. “Not everything that is new is good just because it is new,” he said. “On a national level we will try to proactively educate patients about the different products and options,” said Mr O’Mahony.

The President of the Romanian patient organisation, Mr Daniel Andrei, asked participants for advice on how to approach his government, saying that it only cares about money. Mr O’Mahony answered that countries like Romania need a product selection body with patients and clinicians represented, and need to make the government see the need and utility of having one group making those decisions.

Mr ten Brundel asked the EHC how it would follow up from this Round Table and the EMA meeting. “We want all products and all options maintained,” said Mr O’Mahony, “We need real treatment options for children, and for all countries like Romania,” adding that the EHC will soon finalise its follow up strategy.

Companies too may have an increased role to play, said Dr Giangrande. “When we met the EMA they pointed out that companies are inefficient with their clinical trials, and that they should ensure their paediatric trials are done more quickly,” he said. The challenge is that the requirements are always changing, replied Mr ten Brundel. Sites have to be pre-approved, the right infrastructure and the right clinicians also have to be in place, he said. The EHC could possibly assist with this by helping to prepare countries for new clinical trials, offered Dr Giangrande. Mr O’Mahony agreed that the EHC could take on the role of educating national leaders about clinical trials and including relevant information on its website.

The next EHC Round Table will take place on October 17, 2013 at the European Parliament in Brussels.

All presentations mentioned in this report are available at the following link:
http://www.ehc.eu/round-table-of-stake-holders/last-round-table.html