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"Crazy" European Orphan Drug Pricing System Has To End

by Maureen Kenny

Eurordis head Yann Le Cam outlines his vision for the future of orphan drug pricing in Europe.

EU member states clubbing together to negotiate orphan drug prices with pharmaceutical companies. Lower costs per patient treated but member states guaranteeing immediate and full access, and therefore higher volume sales and faster return on investment. Drug prices fluctuating according to the value of the product in the market at a given time, based on data collected from real-life clinical use after marketing authorization. Differential pricing adjusted according to the number of citizens to be treated or function of GDP. Centers of excellence linked across Europe into "reference networks" where patients would go for clinical trials and treatment access, collecting this real world evidence and actively participating in value appreciation.

This is all part of the vision that Yann Le Cam, the chief executive officer of Eurordis, the European Organisation for Rare Diseases, has for the future of orphan drug pricing and patient access to orphan drugs in Europe. Le Cam, who has just been appointed as a patient representative on the European Medicines Agency's *management board*, outlined his vision to the Pink Sheet's Maureen Kenny.

Eurordis has long argued that the current model, where new and badly needed drugs are approved for marketing by regulators but never get to patients because payers decide they are too expensive, is unsustainable for everyone involved: regulators, national health systems, patients, health technology assessment (HTA) bodies and the industry itself. An innovation that doesn't reach the patient is not a treatment, just an invention. Put simply, says Le Cam, Eurordis *wants* "more, better, cheaper treatments that are available faster". "We want an EU orphan drug pricing system which would mean lower prices [per unit] for companies but member states would guarantee full access," he says. The current system is "crazy" and, according to Le Cam, its days

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Yann Le Cam, chief executive officer of Eurordis

are close to being numbered.

Joint Pricing Negotiations

With regard to joint drug pricing negotiations, some EU member states are clearly attracted by the "strength in numbers" argument. Austria is joining an existing coalition of Benelux countries that is piloting an approach espoused by Eurordis and based on what the association says are the three "core principles" of value assessment, volume of patients treated, and the continuous post-approval generation of real-world evidence. (Also see "*European Pricing Coalition Gathers Momentum*" - Scrip, 23 Jun, 2016.)

The coalition currently comprises Belgium, the Netherlands and Luxemburg. Other countries with "an interest" in joining in addition to Austria include, says Le Cam, Italy, Portugal, Malta and Romania. There are more, but these are the ones he feels at liberty to mention. Through such collaboration, there is a rational for member states to gain capacities (expertise, negotiation, patient access) while re-balancing the power of global companies with local payers constrained by regional EU economic incentives.

Le Cam accepts that larger EU countries such as the UK and Germany with strong purchasing power of their own would have little to gain from collaborative schemes such as these. (Also see "*Benelux Price Negotiations: Beware of EU-Wide Pricing Policy, warns Germany*" - Scrip, 5 Nov, 2015.)

He is, however, in no doubt of its attraction for smaller countries that, individually, have little bargaining power. "We're talking about very small markets. What are you negotiating when you have just two... or three or perhaps ten patients in your country with a specific disease and matching the therapeutic indication?"

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The practice of international reference pricing has to end, says the chief executive officer of Eurordis, Yann Le Cam. This simply encourages member states to look for a price lower than the price their neighbors are paying.

EU Council Conclusions

Eurordis views the Benelux coalition as a welcome development. Indeed, in May this year, the group and the European Patients' Forum *asked* the authorities in the coalition countries to extend their agreement for joint orphan drug price negotiation to other member states that have expressed an interest in such an approach. (Also see "*Orphan Drug Pricing: More Dialogue And Collaboration Needed, Says EURORDIS*" - Scrip, 16 Jun, 2016.)

Le Cam is therefore heartened by the recent recommendation by EU health ministers that member states consider initiatives such as voluntary joint price negotiations as a means of tackling what they say are "very high and unsustainable price levels" that are hindering patient access to effective and affordable medicines. (Also see "*'Skyrocketing' Drug Prices, Access And Availability In Line For EU Scrutiny*" - Pink Sheet, 20 Jun, 2016.)

Under the auspices of the Council of the European Union, EU health ministers last month highlighted their concerns about the financial effect the arrival of high-cost products for diseases such as hepatitis C and cancer is having and will continue to have on national health care systems. The council called on the European Commission to look into the impact of incentives such as data exclusivity, market exclusivity and patent term extensions on innovation, drug pricing, and access to medicines, including generics.

"There are things that we like [about the *council conclusions*] and things we don't like," Le Cam says.

On the positive side, Le Cam views the conclusions as "recognition at the highest political level that the pharmaceutical industry's current business model and the approach to reimbursement from payers and member states are not sustainable."

The council conclusions make it clear that drug pricing and reimbursement decisions are fully the responsibility of individual members states and that any voluntary cooperation between member states "should remain member states driven". "The money stays at national level", says

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Le Cam, but he sees "real goodwill" among member states to find a solution. The fact that they accept that much can be done at EU level is "a big step", says Le Cam, "It means they are trying to find an alternative to just saying no".

Adaptive Regulation

The drug regulatory system is integrated at EU level, health technology assessment is "getting there progressively", but for payers, integration has really "not even started", says Le Cam.

I put it to Le Cam that there is a simple reason pricing and reimbursement authorities are reluctant to join regulators and health technology assessment bodies in early joint discussions regarding potential new products. They fear that if they commit too much early on, they may end up with financial consequences that they simply can't bear. That is fair comment, says Le Cam, but it is not the answer. "The more adaptive we are in the regulatory process, the more we will need collaboration on HTA and pricing at the European level. [Otherwise] we will not solve the issue of access," he says. If we are to get badly-needed new medicines to patients earlier, "everybody needs to take more risk".

On the *negative side*, Le Cam is unhappy at what Eurordis says is the "disproportionate focus" the council conclusions place on the incentives foreseen by existing EU legislation for the development of innovative medicines, particularly those in the Orphan Drug Regulation (Regulation EC 141/2000) and the Paediatric Regulation (Regulation EC 1901/2006). The implied view that such incentives could form part of the problems around access and affordability that are observed today is short-sighted and inaccurate, Eurordis argues. Indeed, the association maintains that the incentives contained in the orphan drug regulation "are the very reason this ground-breaking legislation has proved to be a genuine success in research and innovation, and has helped bring to market 200 therapies for rare diseases since 2000, with or without orphan status".

The way forward, argues Eurordis, is that "all parties need to agree that the real added value of an orphan drug can only be demonstrated through the continuous generation of real-life evidence in the years following marketing authorization and all along the life cycle of the medicine." The future, then, says Le Cam, will involve concepts such as conditional pricing and managed entry agreements, or payment based on patient outcomes, with drug pricing being re-assessed at flexible time points based on additional evidence generated. The more we go down this route, "the more we will need to link what we are paying... with post-market evidence generation", Le Cam says.

How Would It work?

So how would it work? For starters, says Le Cam, the practice of international reference pricing has to end. This simply encourages member states to look for a price lower than the price their

neighbors are paying, he says.

The Eurordis CEO gives an example. A coalition of countries agrees with the manufacturer a transactional price for a new orphan drug product. The price can still be high, but when the drug first hits the market in a small cohort of patients, for example, the company would discount in relation to the degree of uncertainty involved. The discount could be as high as 50%. The company would collect real-world evidence in the intervening period and then come back three years later, say, and – assuming the outcomes merit such a step - increase the price of the drug.

For evidence generation, both patient population size and time counts. To be able to collect data rapidly in the initial phase after approval, member states will need to guarantee access. The aim is to provide the widest possible access to patients while at the same time providing certainty and stability for payers and companies alike. The financial details would be embedded in a contract. Differential pricing could apply, with specific price levels determined by the GDP of the countries involved.

Differential pricing is already a reality in today's orphan drug European market, says Le Cam, but what member states currently pay is unrelated to GDP or national health care budgets per capita. According to Eurordis, a more core co-ordinated and fairer approach to differential pricing is supported by a growing number of payers, industry, patient groups and policy makers. Le Cam believes it can become a reality if it’s associated with the negotiated/agreed price at European level.

Issues such as these are being discussed on various platforms, including under the Mechanism of Coordinated Access to Orphan Medicines or MoCA, which has been established as part of the EU Platform on Corporate Responsibility in the Field of Pharmaceuticals launched by the European Commission in September 2010. (Also see "*Orphan Drug Pricing: More Dialogue And Collaboration Needed, Says EURORDIS*" - Scrip, 16 Jun, 2016.)

Role For Industry

Le Cam wants EFPIA, the body representing R&D-based pharmaceutical industry associations and companies in Europe, to take a more active part in the debate on the future of drug pricing in Europe. "We're asking [EFPIA] not to be reactive," says Le Cam. "We are telling them: Get involved, make proposals. We agree that the current model is not sustainable, potentially killing investment and therapeutic innovation. Together we need to find innovative processes creating value for all stakeholders"

The industry can be conservative and do what it did in the case of the debate on health technology assessment, ie “wait five years then get involved”, or it can be proactive, progressive and liberal and get involved now.

EFPIA has in the past resisted the idea that adaptive pathways to market will lead to lower drug prices. It is wrong to do so, says Le Cam. "If you approve a product at the end of Phase II, the cost to the company of developing the product has been reduced. Fewer patients will have been involved in trials and investment costs will have been lower," he says. Industry should invest the money saved in developing other drugs, Le Cam suggests.

Le Cam has no problem in principle with high prices. In some situations there is an obvious high value, an extremely small number of patients and a small impact on the healthcare budget, and so companies can claim a high price, he says. In other cases, though, there is less certainty and so "the company should no longer demand a high price".

Eurordis is adamant that under the new European approach that it is advocating for, drug companies must be more transparent. "Greater efforts are needed from the pharmaceutical industry to openly justify that the prices assigned to their medicines reflect the true cost of innovation and a commitment to long term sustainable development of new medicines rather than a short term, quick return in pursuit of maximum profit," the group *argues*. "The system is ready to reward innovation," says Le Cam, but it needs co-operation and "a certain openness on costs" from industry as part of the deal.

"Denying the ability of companies to be more transparent, or pretending that information on cost is opposed to the concept of value-based pricing, is a smoke screen, and is hard to accept when talking about a product with a high price, even worse if it comes with high uncertainty. We are not talking mass market here, but highly differentiated niche markets and the only buyer is a public payer". Eurordis compares this resistance from industry to industry's opposition to the transparency on ongoing clinical trials in the 1990s, or to information on negative results of clinical trials being made public in the 2000s.

There's a resistance to change in certain parts of the industry that doesn't help, Le Cam says. Some companies on an individual level are interested in negotiating joint pricing deals on orphan drugs or gene therapy products, he says, but others fear that if they engage at all, the idea "will spread and apply to everything". Some companies have told Le Cam that they'd be willing to lower their prices if they can have a guarantee that every patient who will benefit from the drug will be given it, resulting in fast access and quick generation of data.

Le Cam challenges EFPIA to respond to the *position statement* on access, value, pricing and sustainability with regard to orphan drugs that Eurordis and the European Patients Forum have just released. "Proposing price based on outcome is very interesting but only one part of the solution and it is surely not *the* solution for rare diseases. If it takes two years to discuss each potential innovation in the market access process, we may need 20 years before a new system is in place," adds Le Cam.

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Industry leaders are beginning to engage on the matter but EFPIA has yet to engage as an association. (Also see "*Jimenez: "Huge Sense Of Urgency" To Implement Outcomes-Based Systems In Europe*" - Scrip, 27 Jun, 2016.) (Also see "*Witty On Pricing: Oncology 'No Safe Haven'*" - Scrip, 19 Apr, 2016.)

Le Cam appreciates that it is not easy for EFPIA to come up with one single position that will satisfy the association's diverse membership. EFPIA for its part told the Pink Sheet it was "looking into the pricing issue and how it can support the sustainability of health care systems in Europe".

Joint Procurement Mechanism Not The Right Instrument

An EU framework on a joint procurement mechanism was adopted last year and there was talk of it being used to negotiate pan-EU drug prices. This, however, is not the right instrument for orphan drugs, says Le Cam. "We had thought that might be the way forward but it's not. By definition [with orphan drugs] you have only one product. You cannot do a call for tender and compare offers because you'll only have one offer." Once the period of marketing exclusivity that comes with orphan drug designation has expired and generic versions are available, "then we might want to do that", but not before, Le Cam said.

When Could It Happen?

How realistic is Le Cam's vision? The Eurordis CEO is optimistic. There is no question that today's reality of high starting prices from the industry under pressure from their investors, and payers under pressure from demography and health economics who always want to go down on pricing, "has to change," says Le Cam. "Profits, innovation, access and solidarity should not be opposed; Europe has to help shift to a new model, which in addition will have the potential to spread treatment to other parts of the world."

So how long might it take? The Eurordis chief executive answers with little hesitation: "We'll look back in ten years' time and wonder why we had such crazy drug pricing systems."