# Kluwer Patent Blog

## Controversy in the Netherlands about Novartis orphan drug pricing

Kluwer Patent blogger · Thursday, February 7th, 2019

In the Netherlands, Minister for Health Care Bruno Bruins clashed with Novartis last month about lutetium-octreotaat, after the Swiss pharma company had fivefolded the price of this cancer drug, an ‘orphan medicine’ for patients with neuroendocrine tumors. It is the latest of a series of controversies about medicine pricing. Kluwer IP Law discussed the case with Ellen ’t Hoen, researcher at the Global Health Unit of the University Medical Centre at the University of Groningen and director of Medicines Law & Policy. Novartis reacts at the bottom of this article.

The price hike for the medicine, branded as Lutathera, was described in an article in the Dutch Medical Journal (Nederlands Tijdschrift voor Geneeskunde, NTvG). Researchers of the Rotterdam Erasmus Medical Center have developed lutetium-octreotaat and used it since the year 2000 for the treatment of over 1500 patients (including Apple CEO Steve Jobs).

In 2001 they had formed a startup, Biosynthema, which was sold to the French company Advanced Accelerator Applications (AAA) in 2010 for 10,7 million euros. After additional research until 2015 (amounting to 40 million euros, of which 15 million was paid with French R&D subsidies), AAA obtained registration for lutetium-octreotaat as ‘orphan medicine’, which entails market exclusivity (for 7 years in the US and 10 years in the EU).

According to the NTvG article, the European Medicines Agency approved lutetium-octreotaat for the European market in 2017, and early 2018 Novartis bought all AAA shares for 3,3 billion euros, increasing the price for the product from 16.000 to 92.000 euro per treatment (of four infusions).


Ellen ‘t Hoen

Ellen ‘t Hoen, who has published a lot about medicines law and policy issues, points out this is only the latest example of extremely high pricing of a medicine that used to be available at a much lower rate. ‘Another case that made headlines recently is chenodeoxycholic acid (CDCA), a medicine for the treatment of cerebrotendinous xanthomatosis (CTX), a rare metabolic disease. CDCA is cheap to produce and was on the market from 1976 until at least 2008 under the brand name Chenofalk for the treatment of gallstones. The Chenofalk product cost 0,28 euro per capsule. Since

1999, Chenofalk was used off-label for the treatment of CTX and the price for one-year treatment was 308 euro. After Sigma-Tau Pharmaceuticals (which later became Leadiant Biosciences) acquired the rights to Chenofalk, the product was taken off the market in 2015.

In 2017, the European Medicines Agency approved Leadiant's CDCA for the treatment of CTX. Leadiant brought the product back to market and raised the price to 153.300 euro per patient per year. Because Leadiant also obtained orphan drug designation for the product, the company benefits from ten years market exclusivity in the European Union.

*In the case of lutetium-octreotaat, the Dutch Minister Bruins reacted with disapproval and had what he called an 'intense meeting' with Novartis on 11 January 2019. Afterwards, he stated Novartis hadn't been able to clarify the reasons for the enormous price difference. He also said he made clear he is not willing to pay the price. Novartis however, has not lowered it. What are his options?*

'Academic hospital pharmacists that have been preparing the product will continue to do so and provide this to the patients treated in their centers. This is allowed in the Netherlands, however this does not offer solutions for patients elsewhere. Moreover, concerns about the supply of the raw materials remain since Novartis also owns the producer of these.

What is really urgently needed is a revision of the EU Orphan Drug Regulation to stop the appropriation of old products and products that have been used off label for orphan drug indications'.

*The pharma industry often argues the prices are a consequence of huge investments in research. Is that correct? Are medicines, such as the ones mentioned above, so expensive because they are so sophisticated?*

'The high prices or increase of prices of medicines that used to be affordable is not because they are more sophisticated (some of these products are actually quite simple to make), but because the manufacturer has or has obtained market exclusivity, for example through the EU Orphan Regulation. For the cases here described the increase can only be explained by the fact that the company obtained a monopoly position.

What is needed is much greater transparency with regards to pricing and cost of drug development so that innovation can be fairly awarded and prices set at levels our societies can afford. In the Netherlands the Pharmaceutical Accountability Foundation, which was established last year to address unreasonably high medicines prices, requested the Netherlands Authority for Consumers and Markets to look into the price hike for CDCA and whether Laediant is abusing its dominant market position (see also here).'

*Do you think Novartis or pharma more in general is impressed if Minister Bruins says that the industry should take its social responsibility?*

'No, companies have been told this for decades. There are even UN norms for the pharmaceutical industry that set out their core human rights obligations. Perhaps individuals in a company may want to listen, but the company as such will first and foremost respond to the shareholders who demand the highest possible returns. High drug prices are a global problem. See for example the

CDCA case in Belgium. The UK rationed the hepatitis C treatment for cost reasons as well as breast cancer treatments for some time. And recently a group in Switzerland has asked the government to issue a compulsory license for a breast cancer drug because of excessive pricing.

*Would you like to see a change in (international) legislation? Do patent laws in general and regulations such as the Orphan Drug Regulation have the effect governments aimed for?*

'In the two cases CDCA and Lutathera, patents were not the problem but exclusivity granted through the regulatory system.

In the short term I would like to see governments take action when patents stand in the way of accessing medicines for which the patent holder refuses to propose a reasonable price. In the EU this can be done by amending the EU medicines regulatory network to allow waivers to data and market exclusivity in cases of public health need and when a compulsory or government use license has been issued (see also here).

The EU Orphan Drug Regulation needs to be amended to stop the kind of abuse that is illustrated by the CDCA and Lutathera case, where companies take old drugs and obtain a market monopoly.

In general the proliferation of exclusive rights, patents, SPC, data and market exclusivity should be reviewed and revised in the EU to ensure affordability of care. Greater transparency with regard to R&D cost and pricing should be implemented and form a basis for decisions on how best to remunerate innovation.

At the core of the problem is the idea that granting market exclusivity is the best way to encourage innovation. This has never really been examined. Looking at what we pay for new medicines these days, paying directly for innovation in a so-called delinkage model may be a much more efficient way of getting what we need.

*Is this a far horizon or do you see or expect concrete steps in this direction at the EU or international level?*

'The crisis of high priced medicines is taking place now and is global. Solutions to this crisis should not be on a far horizon but be explored and implemented with a sense of urgency. The review of the EU incentive mechanisms is an important first step that should lead to revision of the rules to better balance access with innovation.'

**REACTION NOVARTIS:**

*There are two different products available in The Netherlands and there has been no price increase to either one. Advanced Accelerator Applications (AAA), a Novartis company, provides two offerings in the Netherlands:*

- *Lutathera®, the first ready-to-use Peptide Receptor Radionuclide Therapy (PRRT) ever approved by the EMA and FDA that includes a targeting molecule (dotatate) attached to a radioactive component (lutetium 177/Lu-177); and*
- *Lutetium 177 (Lu-177), the radioactive component of Lutathera, which certain hospitals in the Netherlands use to make their own PRRT using Lu-177 – purchased from either a subsidiary of AAA called IDB or from other suppliers – plus the targeting peptide purchased from other sources.*

*The articles published in the Netherlands were comparing estimated costs of the PRRT produced by certain hospitals for their individual patients with the cost of Lutathera, a "ready-to-use" drug that has received marketing authorization in the EU and US and is being made broadly available.*

*For the handful of hospitals in the Netherlands that have the capability to prepare their own treatment, Lu-177 remains available, with no price increase. But it's important to keep in mind there are also many other hospitals in the Netherlands and across Europe and the United States that don't have the ability to prepare their own treatments. So it's important that EMA- and FDA-approved Lutathera is also available to patients.*

*Lutathera has been approved for reimbursement in the Netherlands and we are currently in negotiations on price. We recognize the special role of the Erasmus University Medical Center in Rotterdam in the early development of PRRT. We have engaged in constructive dialogue with all relevant stakeholders in the Netherlands including the government and payers and we are working together on finding a solution.*

***Additional background***

*AAA conducted a global Phase III trial of Lutathera, negotiated with regulatory authorities, has established a global GMP-certified manufacturing process to produce ready-to-use drug, and developed a global supply chain process that allows us to deliver Lutathera to hundreds of centers in Europe and the US that lack the ability to make it themselves. We are committed to doing everything we can to ensure access for patients who may benefit from this innovative therapy.*

*The price of Lutathera was carefully considered and based on the benefit the treatment provides to patients, healthcare systems and society at large. It is priced comparably to other existing therapies approved for this patient population. Lutathera is widely reimbursed in the US and several EU payers already have reviewed and recommended Lutathera for reimbursement based on their evaluation of its efficacy and cost-effectiveness. Several other EU countries are currently conducting these evaluations as well.*

---

This entry was posted on Thursday, February 7th, 2019 at 2:18 pm and is filed under Netherlands, Pharma, Pharmaceutical patent
You can follow any responses to this entry through the Comments (RSS) feed. Both comments and pings are currently closed.