Six Degrees of Separation

Market Analysis of Catalyst Pharmaceutical's Firdapse price hike

February 14, 2019

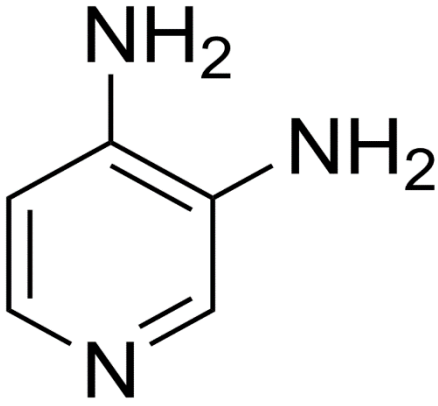
You struggle to get out of your chair or climb stairs due to muscular weakness. You're always tired and fatigued. You frequently experience symptoms such as blurred vision, constipation, a dry mouth, hypotension and impaired sweating. Your body is attacking its own nerve endings. You are living with Lambert-Eaton Myasthenic Syndrome. Chances are, you will only get weaker and more fatigued over time.

With this in mind, it sure is nice to know that thanks to the Orphan Drug Act of 1983, both the government and drug companies such as Catalyst Pharmaceuticals have your back, working together to develop a treatment to alleviate your condition and dramatically increase your wellbeing.

That is, until the price tag of $375 000 per year hits you like a slap to the face.

You used to receive a similar treatment for free. Now you discover that Catalyst Pharmaceuticals has purchased the rights to this critical drug just so they could profit from your suffering. There is no other explanation for the unworldly price tag, unless Catalyst Pharmaceuticals have concluded that LEMS only afflicts millionaires.

In any other case of such blatant price manipulation and monopolization, there would be a riot. Catalyst has leveraged the patent and orphan drug protection systems to exploit vulnerable patients and taxpayers alike.



All this fuss over 3 nitrogens and 4 hydrogens? Image source: Edgar181 [Public domain], from Wikimedia Commons

For many years, the Orphan Drug act of 1983 has been used to help deliver lifechanging and lifesaving treatments to patients dealing with conditions that are so rare that it would not be commercially viable for pharmaceutical companies to develop treatments for them. Through providing the developers of orphan drugs tax breaks, extra market protection, and other taxpayer-funded benefits, the act has been widely described as a success, with the number of orphan drugs developed increasing exponentially after the implementation of the act. One of these drugs sponsored under the act is 3,4-diaminopyridine, also known as Amifampridine or **Firdapse**. In its base form, 3,4-DAP has been to treat LEMS and other Myasthenic syndromes for over 20 years and was available **free of charge.**[1] While there have been many success stories under the act, this is slowly changing as companies like **Catalyst Pharmaceuticals**, determined to exploit the system, **use this act to fleece taxpayers AND vulnerable patients** at the same time. Catalyst Pharmaceuticals purchased the rights to 3,4-DAPP, a variation of 3,4-DAP, in 2012 and upon receiving FDA approval for this drug under the name Firdapse on the 28th of November 2018, they have set the list price at **$375,000 per year of treatment**[2] which is astronomically unaffordable for most patients and blatant appropriation from taxpayers. Catalyst pharmaceuticals did **NOT** discover the drug and they did **NOT** develop it - at best they can claim that they funded the clinical trials and FDA approval process. Keep in mind that throughout this process, they have had the benefit of the orphan drug designation, meaning the government has subsidized and simplified the process of approval for Catalyst. After receiving government assistance and funds to develop the drug, it is total misappropriation of the spirit of the original act and exemplifies corporate greed at its worst to turn around and exploit the vulnerable for profit.

[1] https://clinicaltrials.gov/ct2/show/NCT01511978
[2] https://catalystpharma.com/wp-content/uploads/2018/12/Final-Transcript.pdf

Analysis

To better understand the situation, we used our proprietary analytical systems to research Catalyst's patent portfolio containing the patent for 3,4-DAPP. Given the mysterious absence of their own invention – the justification pharmaceutical companies and their industry associations use for justifying exorbitant pricing – our review prompted a background check of the history of license transferal. The next searches for Biomarin, Huxley, EUSA, OPI yielded similar results, until finally the sixth search yielded a result. The story that follows is no less than a saga.

Assistance Publique Hôpitaux de Paris – the Public Assistance Hospitals of Paris (APHP) - is a university hospital trust based in Paris and surrounds. It is the largest hospital system in Europe, one of the largest in the world, and provides a wide range of services and facilities, including research and development of new drugs. Most notably for the purposes of this report, they developed two novel compounds for the treatments of Myasthenic syndromes - 3,4-diaminopyridine tartrate (3,4-DAPT) and phosphate (3,4-DAPP).

Four French researchers from the hospital are named on a 2001 French patent[3], which as far as our research has shown, appears to be the first and main patent protecting the drug Firdapse. Filed on the 5th of February, it will be expiring on that date in 2021 – just under two years from now. 3,4-DAPP has proved to be a successful treatment for many forms of Myasthenic syndromes which thousands of patients around the world rely on for treatment.

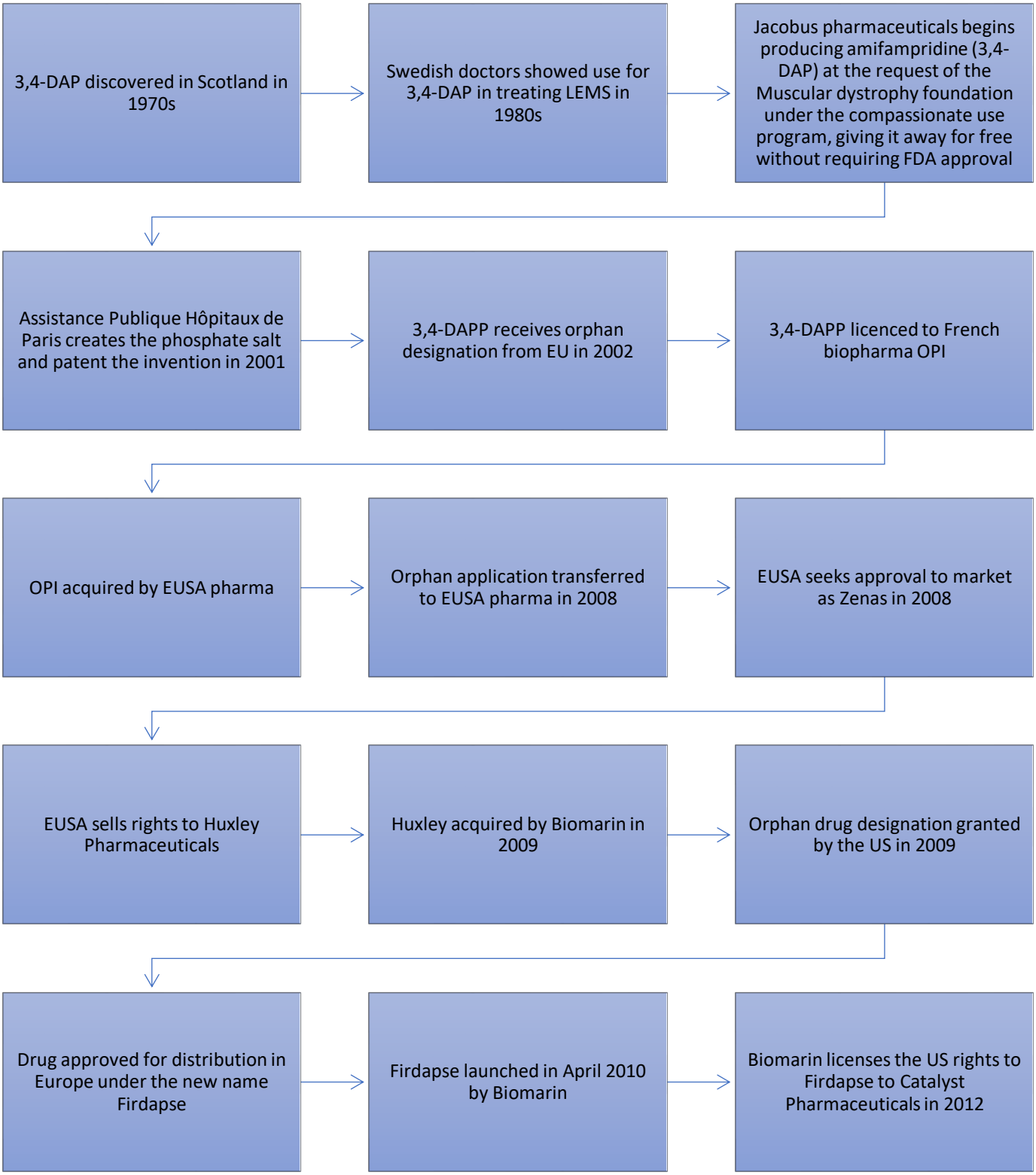
Interestingly enough, before the French patent in 2001, 3,4-diaminopyridine appears in several patents related to various chemical processes, and even in hair product patents from L'Oreal. The idea of using 3,4-diaminopyridine for medical purposes goes back to the 80s, so this is by no means a new invention. The key factor in the 2001 patent is the idea of using it with commonly known salts to stabilize the compound's delivery. This was the breakthrough that gave it a useful shelf life and viability as a commercial drug. Jacobus Pharmaceuticals had been making 3,4-DAP in its free base form (not the salt) since the 1990s, and did so for around 20 years, giving it away for free under the compassionate use program – a program which allows pharmaceutical drugs to give away experimental drugs for free rather than having to pay for expensive trials to get FDA approval.

Fast forward to 2019, and you may now have seen on the news this so-called scandal[4] involving Catalyst Pharmaceuticals. It really entered the public sphere of consciousness when Senator Bernie Sanders wrote an open letter to Catalyst[5], accusing them of setting a "staggering list price" and "…not only a blatant fleecing of American taxpayers, but … also an immoral exploitation of patients who need this medication."

Sadly, this isn't even the first time this is happening with 3,4-diaminopyridine. In 2010, when Biomarin acquired the rights to 3,4-DAPP, they pulled a similar stunt to Catalyst, taking a drug they hadn't developed and hiking the price up to receive massive profits, receiving $10.8 million in the first 9 months of 2012[6]. A group of British neurologists and pediatricians send an open letter to David Cameron asking him to review the situation, worried that the increased price would adversely affect patients. Sound familiar?

[3] FR2820423
[4] https://www.cnn.com/2019/02/04/health/bernie-sanders-firdapse-catalyst-bn/index.html
[5] https://www.sanders.senate.gov/download/letter-to-catalyst?inline=file
[6] https://www.bizjournals.com/sanfrancisco/blog/biotech/2012/10/biomarin-catalyst-firdapse-lems.html

The background of the current situation in the US is equally complicated. Below is a summary of the events leading up to Catalyst licensing Firdapse:



Further Complications – Orphan Drugs

Further complicating matters is the fact that 3,4-DAPP is classified as an orphan drug in both Europe and the United States. Orphan drug status is granted to drugs developed to treat orphan diseases, which are diseases so rare and affecting so few people, that it is not commercially viable to develop a treatment for them, as the volume of demand for any treatment would be too low to cover the cost of development. To combat this, many governments have implemented orphan drug programs which counter this problem by extending extra market protections and financial benefits to the developers of orphan drugs in order to make them financially viable and develop treatments for diseases that would otherwise go untreated.

Under the Orphan Drug Act of 1983, which has later been adopted by Japan and the European Union, the sponsor of an orphan drug is entitled to tax benefits, lower testing volume requirements, and extra market protection – specifically, 7 years from the date of approval[7]. Different to patent protection, the orphan drug designation blocks FDA and government approval for the drug by anyone but the sponsor for seven years.

To qualify as an orphan drug under the act, it either has to be a treatment for a disease affecting less than 200 000 Americans, or more than 200 000 cases but with no reasonable expectation of profits for development. Based on the statistic of roughly 20 cases of Myasthenia Gravis per 100 000[8] (there are only about 400 cases of LEMS in the US, so this can be considered insignificant), it works out to roughly 65 000 patients living with myasthenic syndromes. However, one could argue that the cutoff is rather arbitrary and there should be more focus on the expectation of profits, especially in cases such as this. When a drug with an orphan designation is being sold at a farcical price, the designation should be revoked, as clearly the market protection is being exploited.

Image © 2019 Nicolas Wales

This is an especially poignant argument when companies who have not participated in the majority of the development of the drugs are reaping in the profits. 3,4-DAPP, having been transferred five times before being in the hands of Catalyst Pharmaceuticals, can hardly be described as a drug where Catalyst has spent years developing the drug, since they licensed the drug 11 years after it was first discovered and developed. There has been public concern for a while that cases like this are exploiting the Orphan Drug Act in ways not imagined or intended by the original act.[9]

Unfortunately, while the 7-year market protection afforded by the orphan status sponsored by Catalyst for 3,4-DAPP to treat LEMS has expired, they have received two other designations – for treating myasthenia gravis (licensed in 2016), and congenital myasthenic syndromes (licensed in 2015)[10]. These two are far greater in volume of cases than LEMS and would contribute to the bulk of potential profitability of a generic drug substitute. This has been described as "double dipping"[11] and is yet another issue that the Orphan Drug Act faces.

[7] https://www.law.cornell.edu/uscode/text/21/360cc
[8] http://myasthenia.org/WhatisMG.aspx
[9] https://www.npr.org/sections/health-shots/2016/09/07/493000612/how-much-do-drugs-for-rare-diseases-add-to-health-care-spending
[10] https://www.hrsa.gov/opa/program-requirements/orphan-drug-exclusion/index.html
[11] https://www.healthline.com/health-news/critics-orphan-drug-law-ripe-for-abuse#4

Document #	Title	Assignee Name	Priority	File	Issue
US20150353467	3,4-DIAMINOPYRIDINE TARTRATE AND PHOSPHATE, PHARMACEUTICAL COMPOSITIONS AND USES THEREOF	ASSISTANCE PUBLIQUE - HOPITAUX DE PARIS	20-Jan-04	5-Aug-15	10-Dec-15
US20140080875	3,4-DIAMINOPYRIDINE TARTRATE AND PHOSPHATE, PHARMACEUTICAL COMPOSITIONS AND USES THEREOF	ASSISTANCE PUBLIQUE-HOPITAUX DE PARIS	5-Feb-01	20-Nov-13	20-Mar-14
US20040106651	3,4-diaminopyriding tartrate and phosphate, pharmaceutical compositions and uses thereof	ASSISTANCE PUBLIQUE-HOPITAUX DE PARIS	5-Feb-01	20-Jan-04	3-Jun-04
EP1358159B1	3,4-DIAMINOPYRIDINE TARTRATE AND PHOSPHATE, PHARMACEUTICAL COMPOSITIONS AND USES THEREOF	ASSISTANCE PUBLIQUE-HOPITAUX DE PARIS	1-Feb-02	22-Jul-09	22-Jul-09
FR2820423	TARTRATE ET PHOSPHATE DE 3,4-DIAMINOPYRIDINE, COMPOSITIONS PHARMACEUTIQUES ET UTILISATIONS	ASSISTANCE PUBLIQUE HOPITAUX DE PARIS Etablissement public	5-Feb-01	2-Dec-05	2-Dec-05
US20140255380	METHODS OF ADMINISTERING 3, 4-DIAMINOPYRIDINE	BIOMARIN PHARMACEUTICALS, INC.	30-Jun-11	29-Jun-12	11-Sep-14
WO2013003708	METHODS OF ADMINISTERING 3,4-DIAMINOPYRIDINE	BIOMARIN PHARM INC	30-Jun-11	29-Jun-12	3-Jan-13

This is a listing of all of the patents we found relating to Firdapse (3,4-DAPP). There is the original patent family, and then a further patent from Biomarin on methods of administering the drug, which is a potential roadblock to a generic drug, but likely not enough to completely block a generic substitute. Note that there is not actually any current US patent protection, as all of the patents that have been filed in the US are still in the application stage.

Conclusion

This situation highlights the need for orphan drug laws to be reexamined to ensure that they are still being used for their intended purpose: developing drugs for rare diseases that would not otherwise have been developed; and not simply as a vehicle for large pharmaceuticals to exploit and make their drugs more profitable than they otherwise would have been. Used on top of patents, these exclusive market rights can be used to further exclude competitors from making a generic alternative and charging an unreasonably high price for a drug which is critical for many American patients. **The US needs to seriously assess cases like this where we are subsidizing pharmaceutical companies to develop a drug and then allowing the same company to further scam taxpayers by having them pay AGAIN for the same drug set an unaffordable list price.** The patent system and the orphan drug system are now stifling innovation and development, rather than encouraging it as they were originally intended to do.

With regards to 3,4-DAPP in particular, it will be interesting to see if the US patents are granted or not. If they are, the protection life span of Firdapse may be very significant and it may be a long time before a generic competitor can be produced. If this is the case, the “staggering list price” is even more unjustified.

This is an unfortunate case of a string of pharmaceutical companies doing a good job protecting their IP and using their protected position to fleece consumers. Clearly, the orphan drug act needs to account for profits on orphan drugs, and perhaps revoke orphan status once the drug breaks through a profitability measure. Otherwise US taxpayers are simply helping to bankroll the extortion of vulnerable patients relying on a life-changing treatment for their condition.

One silver lining here is that the drug is not protected outside of Europe and the US and could be freely developed and sold in many other markets like Australasia, Canada, and South America

For more details on this report, please contact patentlyobvious@m-cam.com.

A Brief Primer on the Patent System

In recent years, the importance of patents and intellectual property rights as an important variable in the marketplace has come to the forefront of the public consciousness as world leaders declare their country's lead in the innovation race. Damaging intellectual property litigation is becoming increasingly common across all industries. This is exacerbated when patent rights are granted for non-novel ideas. A vast amount of precedent innovation is unconsidered by patent-granting authorities in the creation of new IP rights. Patent granting authorities including the United States Patent and Trademark Office (USPTO), European Patent Office (EPO), Japanese Patent Office (JPO), Chinese State Intellectual Property Office (SIPO), Korean Intellectual Property Office (KIPO) and many others are constrained by the use of patent classification systems which are routinely circumvented by patent applicants.

There is a two-way social contract underlying the patent system. In the United States, patent terms are generally limited to 20 years from the date of application. By statutory intention, once a patent has expired, the patent holder loses the right to exclude others from fully utilizing any innovation described in the patent. A large number of patents enter the public domain when they are "abandoned" – when owners discontinue paying patent maintenance fees. Patents also only provide an exclusionary right in the country for which the patent is filed. As demonstrated by the Global Innovation Commons[12] (G.I.C.), using intellectual property available in the public domain eliminates the need to pay licensing fees on those innovations in countries where the patent was never registered, or worldwide, if abandoned.

Patently Obvious® is a report focusing on select groups of patents in order to increase transparency in markets, addressing information asymmetries, and providing a more level playing field for all parties.

[12] http://www.globalinnovationcommons.org/