

Overpatented, Overpriced Special Edition

Lantus

(insulin glargine)



Solving the drug patent problem

Key findings

95% of the total patent applications on the diabetes treatment Lantus in the U.S. were filed by pharmaceutical company Sanofi **after the drug was first approved and on the market in 2000.**

74 patent applications have been filed on Lantus in the U.S., which have the potential **to delay competition for 37 years.**

Sanofi has filed **1.5x as many patent applications in the U.S. than at the European Patent Office**, and three times as many patent applications in the U.S. as in Japan.

Total Medicare and Medicaid spending on Lantus increased 132% between 2012 and 2016, and during that time the average annual Medicare spending on Lantus per person rose from \$1,284 to \$2,431, an increase of 89%.

Lantus insulin has the highest annual price hikes for Medicaid (over 18% per year from 2012-2016) **and second highest for Medicare**, a main reason for the massive public spending on the drug.

The wall of patents that Sanofi has built around Lantus continues to keep competitors' biosimilar products to treat diabetes out of the market in the U.S. **The extent of overpatenting on critical lifesaving medicines like Lantus raises serious questions about whether many issued patents on these medicines are strategically filed to delay competition and if they are actually warranted** – and whether there is a need to revisit patentability standards.

Introduction

In August 2018, the Initiative for Medicines, Access and Knowledge (I-MAK) released **Overpatented, Overpriced**, a report that revealed how drugmakers file hundreds of patent applications in the U.S. – the vast majority of which are granted. Drugmakers have sought, on average, 38 years of attempted monopoly protection through patents and patent applications on these twelve best-selling medicines.¹ Patents are designed to protect inventions for a limited time: 20 years from the time the patent application is first filed. Without the threat of competition, all but one of the medicines we studied has increased in price.² For these eleven other best-selling medicines, the average price increase was 80% since 2012.

This case study on the diabetes drug Lantus (insulin glargine) is the second in a series of in-depth investigations into the best-selling medicines featured in **Overpatented, Overpriced**. Lantus, which is patented by Sanofi, is an insulin analogue used for the management of Type I diabetes and particular cases of Type II diabetes. The global disease burden due to diabetes has risen dramatically over the last decade, particularly in low- and middle-income countries.³ In the U.S. today, over 100 million Americans, or one out of three people, is currently living with diabetes or pre-diabetes; it is especially prevalent amongst minority populations and older Americans.⁴

In total, Sanofi has filed 74 patent applications on Lantus in the U.S. with the aim of preventing competition for a total of 37 years. Sanofi generated \$5.7 billion in sales in 2017, a sign of both the ever-expanding burden of diabetes and of Sanofi's overpatenting and overpricing of Lantus.

When did Sanofi overpatent Lantus (insulin glargine)?

The first patent application on Lantus was filed in 1994.⁵ Subsequently, Lantus was approved by the U.S. Food and Drug Administration (USFDA) in April 2000.⁶ Even if Sanofi had not filed any additional patent applications, the corporation would have secured approximately 15 years of monopoly protection for Lantus in the U.S. on the basis of just the primary patent, which expired in 2015.

Drugmakers often argue that additional patent applications filed prior to regulatory approval incentivize companies to invest in the development of a new drug and should not be characterized as evergreening.⁷ Therefore, we examined how many patent applications on Lantus were filed in the U.S.

¹ <http://www.i-mak.org/overpatented-overpriced-excessive-pharmaceutical-patenting-extending-monopolies-driving-drug-prices/>

² The one drug which experienced a price decrease was Herceptin, a drug which is likely facing competition from biosimilar product(s).

³ <http://www.who.int/diabetes/global-report/WHO2016-Presentation.pdf>

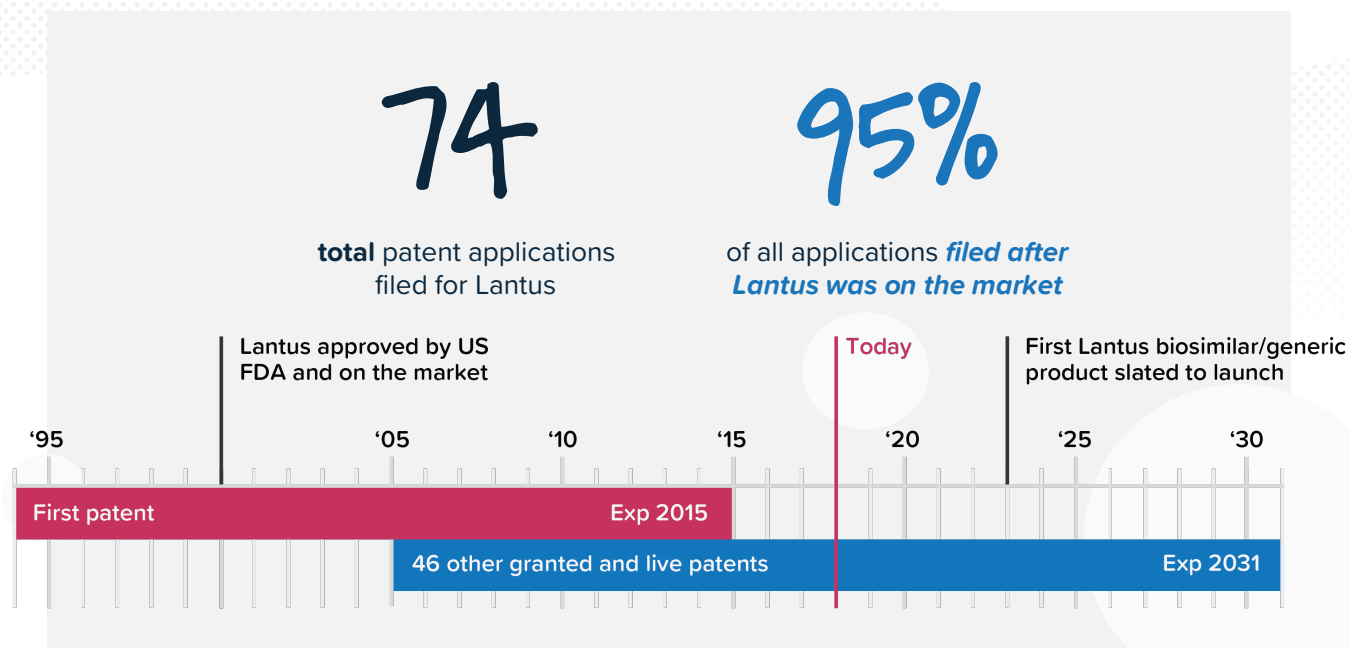
⁴ <https://www.cdc.gov/media/releases/2017/p0718-diabetes-report.html>

⁵ The first patent on Lantus was filed by Hoechst A.G, which was subsequently acquired by Sanofi. Although the filing date for the first patent on Lantus is 1994, the priority claim dates back as far as 1988.

⁶ <https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/619/lantus-insulin-glargine-rdna-origin-injection>

⁷ 9 Evergreening refers to the strategy of a company obtaining multiple patents covering different features of the same product in order to extend

after regulatory approval at the USFDA in 2000. Our research found that 95% of the total patent applications (69 out of 74) on Lantus in the U.S. were filed after the drug was approved in 2000. Presently, the U.S. Patent and Trademark Office (USPTO) has granted patents on Lantus through 2031, more than thirty years after the USFDA approved the drug.



While not all secondary patents impede the introduction of generic or biosimilar products, competitors must still undertake due diligence to identify and examine these patents in order to avoid litigation with the patent owner. This due diligence can amount to a significant transaction cost financially and in terms of time. Many secondary patents do lead to litigation initiated by the patent holder and settlements that delay competitors entering the marketplace. Unsurprisingly, two companies seeking to introduce competition to Lantus in the U.S., including one already with USFDA approval of its own version of insulin glargine, are currently locked in litigation with Sanofi – eighteen years after the USFDA approved Lantus and three years after the primary patent expired.⁸ Merck, the U.S. distributor of a potential competing product already approved by the USFDA but challenged by Sanofi in patent litigation, decided last month to withdraw its launch of the product.⁹

the monopoly period. Patent evergreening is also commonly referred to as "stockpiling", "thickets", "layering", "life-cycle management", or "line-extension".

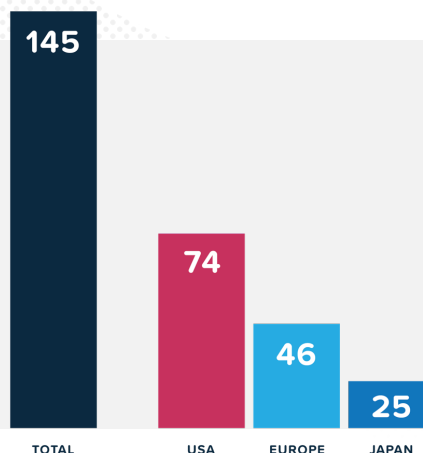
⁸ <https://www.fiercepharma.com/legal/seeking-to-defend-key-sales-sanofi-sues-mylan-for-lantus-patent-infringement>

<https://www.fiercepharma.com/marketing/despite-scoring-fda-nod-merck-follow-med-lusduna-must-wait-to-challenge-lantus>

⁹ <https://www.statnews.com/pharmalot/2018/10/12/merck-biosimilar-lantus-insulin/>

In sharp contrast, I-MAK's research found that Sanofi has filed a total of 46 patent applications to date on Lantus at the European Patent Office and 25 in Japan. This amounts to nearly twice as many patent applications in the U.S. compared to Europe, and three times as many patent applications in the U.S. compared to Japan.

Lantus's 74 patent applications in the U.S. are 1.5x those in Europe, and almost triple those in Japan.



Due in part to more friendly biosimilar regulatory requirements in Europe and Japan compared to the U.S., multiple insulin glargine biosimilars or follow-on biologics have been approved in Europe and Japan since 2014. In the U.S. only one product, a follow-on biologic marketed by Eli Lilly, is the sole entrant and competitor in the U.S. market.

Country / region		Product Name	Active substance	Approval date	Manufacturer
Japan	1	Abasaglar	insulin glargine	26 Dec 2014	Eli Lilly/ Boehringer Ingelheim
	2	Basalog	insulin glargine	26 Mar 2016	Biocon/ Fujifilm Pharma
Europe	1	Abasaglar	insulin glargine	9 Sep 2014	Eli Lilly/ Boehringer Ingelheim
	2	Lusduna	insulin glargine	4 Jan 2017	Merck/ Samsung Bioepsis
	3	Semglee	insulin glargine	28 Mar 2018	Mylan/ Biocon

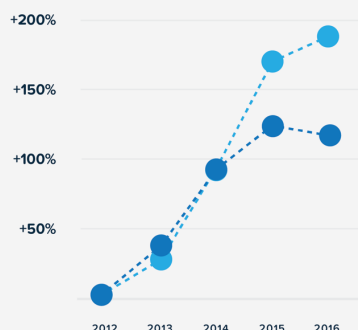
Assessing the financial burden of overpatenting on taxpayers (through Medicare and Medicaid purchases)

The U.S. government pays about 43% of total annual prescription drug costs in the U.S. (\$325 billion), with private insurers contributing a similar amount and the remaining 14% paid by individuals out-of-pocket. Approximately 91% of total government spending on medicines comes from U.S. taxpayer-funded Medicare and Medicaid drug purchases.¹⁰ These agencies play a crucial role in ensuring that Americans have access to necessary medicines and health care.

Over a five year period from 2012 to 2016, taxpayers spent a total of \$22 billion on Lantus¹¹ through Medicare and Medicaid purchases.

Medicare spent \$17 billion on Lantus insulin, more than any other drug for the agency; and the \$5 billion Medicaid spent on Lantus ranked it second in overall drug spending for the agency in that period. **Total spending on Lantus insulin by the two agencies increased 132% between 2012 and 2016.**¹²

Lantus Spending Total % Increases



Medicaid

+188%, from \$533m to \$1.54b

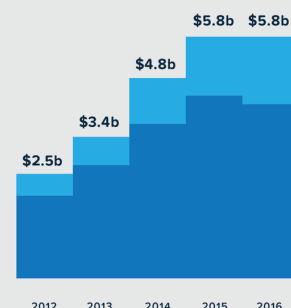
Medicare

+117%, from \$1.94b to \$4.21b

Avg Medicare Spend Per Beneficiary



Total spent on Lantus by Medicare & Medicaid



The huge increase in public payer spending can be largely attributed to price hikes – not expanded use of this diabetes treatment. Medicare reported that Sanofi has increased the price of Lantus by over

¹⁰ These figures represent spending on all retail prescription drugs but exclude those directly administered by doctors and/or in hospital settings. Calculations made from data available at <https://www.brookings.edu/blog/up-front/2017/04/26/the-hutchins-center-explains-prescription-drug-spending/>

¹¹ Includes spending for both Lantus and Lantus Solostar, the pen-based delivery device.

¹² All historical data on Medicare and Medicaid spending sourced from CMS Drug Spending Database, available at: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Information-on-Prescription-Drugs/index.html>

18% *per year* between 2012 and 2016. In just five years, Medicare's average annual spending per person for Lantus rose from \$1,284 in 2012 to \$2,431 in 2016, an increase of 89%. Though more recent public payer data is not yet available, I-MAK's **Overpatented, Overpriced** report found that the price of Lantus has increased an additional 24% from 2016 to 2018.

How much *does* Sanofi make on Lantus?

\$5.7b → **\$15.6m** → **\$651k** → **\$11k**
 P/YEAR P/DAY P/HOUR P/MINUTE

The price increases for Lantus and several other patented competitors in the U.S. market have led to calls for investigations of these pricing practices at both the federal and state levels. Members of Congress have alleged that Sanofi, alongside insulin manufacturers Eli Lilly and Novo Nordisk, were engaged in 'price fixing' due to the strikingly similar prices rises of all three companies' insulin products.¹³ At the same time, state attorney generals and class action lawyers have initiated legal proceedings due in large part to the uncontrolled price rises for Lantus and other patented insulin products.¹⁴

Impact on patients and families living with diabetes

High prices for medicines are not solely an issue of insurance reimbursements, or for the poor who cannot afford them. Overpriced medicines affect all Americans, limiting the ability of the healthcare system to provide patients with necessary medicines. They also tie up taxpayer dollars, which, if freed, could be spent on other priorities.

Sanofi's overpatenting of Lantus insulin has resulted in significant expenditure by Medicare and Medicaid since 2012, but has also had a direct impact on the treatment outcomes and financial well-being of Americans. People living with diabetes may skip or ration doses, leading to weight loss and lethargy, to ensure family members do not have to sacrifice their savings to cover out-of-pocket costs.¹⁵

¹³ <https://www.statnews.com/pharmalot/2016/11/03/sanders-insulin-investigation/>

¹⁴ <https://www.nbcnews.com/health/health-news/several-probes-target-insulin-drug-pricing-n815141>

¹⁵ <https://www.nbcnews.com/health/health-news/several-probes-target-insulin-drug-pricing-n815141>

The story of Erin Little, who is living with diabetes and is part of the diabetes patient advocacy group T1International, is an example of how Americans are negatively impacted by the price of Lantus:

"I have Type 1 Diabetes. As an entrepreneur I do not currently have health insurance. No one I know can afford this drug without assistance, and patient assistance programs, if you even qualify, eventually run out. I had to pay \$1,000 for a month's supply of Lantus before I found a way to get the same version in Mexico for just \$100. It's not right. Drug companies are squeezing us for every possible penny. It's forcing people to ration drugs and putting lives at risk."

ERIN LITTLE, KANSAS CITY, MISSOURI

The reality of the excessive pricing of Lantus is also seen in the stories of Jerrelene Krawetzki and Steven Hadfield, provided by Patients for Affordable Drugs (P4AD), an organization working to reduce drug prices in the U.S.:

"My name is Jerrelene Krawetzki and I'm from Berlin Heights, OH. Because of diabetes type 2, I require Lantus and Humalog. Because of the increased costs of these medications, after filling the first prescriptions, I'm already in the donut hole. This means a one-month prescription of these two drugs will cost over \$600 per month. Senior citizens on a fixed income cannot afford this. Since I've fallen into the donut hole in February, Lantus is \$400 for three months. And that's with insurance. My husband and I have trouble meeting that cost."

JERELENE KRAWETZKI, BERLIN HEIGHTS, OHIO

"I am on three kinds of Insulin as prescribed by Joslin Diabetic Center in Boston Mass. Lantus is my Long Acting Insulin that I take at bedtime. Up until two weeks ago I was on 35 units a night. Now it has been revised to 20 units at bedtime. However, Lantus is very expensive. The cost of a vial of Lantus is \$350. Therefore at the beginning of each year I have to pay full price for each vial. I average two vials per month. Even after you make your deductible the patient pays 25% which is about \$90. I do not always have this money to purchase my needed insulin as I am limited to what I can do. My lifestyle has changed to a lower lifestyle because of not always having funds to take care of my diabetes. Without Lantus I have high Blood

Glucose Readings and my nerves in my legs, feet, arms and hands has already had major damage and I am constantly in pain.”

STEVEN HADFIELD, CHARLOTTE, NORTH CAROLINA

Conclusion

The wall of patents that Sanofi has built around Lantus continues to keep biosimilar products to treat diabetes out of the market in the U.S.

Drugmakers claim that patents are the only incentive to generate new medicines to address unmet needs. However, most of the patents on Lantus were filed *after* the drug was on the market. Patents should be rewarded for genuine inventions. However, the extent of overpatenting on critical lifesaving medicines like Lantus raises serious questions about whether many patent applications and issued patents on these medicines are strategically filed to delay competition and if they are actually warranted – and whether there is a need to revisit patentability standards.

In the Annex to this report, I-MAK has included a set of policy prescriptions to address overpatenting that could be taken forward by Congress and the USPTO. Public participation sits at the heart of effective government regulation. Undertaking reform must first start with public conversations about pharmaceutical patenting practices and their impact on rising drug prices for public and private payers and households across America.

The USPTO should invite non-profit organizations and other experts that represent the public interest in the patent system to have permanent seats on the Public Patent Advisory Committee; and Congress should hold hearings to assess how pharmaceutical patenting practices affect federal health care programs and American families. This will enable Congress to provide effective oversight of the USPTO and other federal agencies that have the authority to address the overpatenting problem.

Until the U.S. government begins to substantively address the issue of overpatenting, American consumers and payers will continue to bear the physical and financial burdens. The U.S. cannot fix the drug pricing crisis until it solves the drug patent problem.

ANNEX

Patent Policy Prescriptions

The epidemic of overpatenting

Filing hundreds of secondary and tertiary patent applications allows brand name drug manufacturers to unfairly extend monopoly protection and keep drug prices high. Some potential policy options to address the problem of overpatenting are:

- Modify the “inventiveness” standard for patents so that non-inventive and commonly practiced techniques in the pharmaceutical field cannot be patented. Raising the bar for the inventiveness standard will likely help curb non-inventive patenting, reduce litigation, and accelerate competition after the intended 20 years of protection that could drive down drug prices.
- Eliminate continuation applications at the USPTO so that a patent applicant does not have unlimited attempts to gain a patent on the same invention even when the USPTO may have made initial rejections. Drugmakers deliberately file continuation applications so they linger in the system as a deterrent for potential generic drug competitors and can eventually lead to multiple patents being granted for the same invention. Removing continuation applications would address a key anticompetitive behavior of brand name drug manufacturers.

Public participation in the patent system

Unless non-commercial actors and other interested parties are sued for patent infringement, they do not have legal standing to challenge patents in federal court. This means that the only recourse for non-commercial actors and other interested parties in the patent system lies at the USPTO.

Some potential policy options to allow for greater involvement of the public in the patent system to help improve transparency and address patent abuse are:

- Maintain and improve the existing patent challenge system, which includes the Inter Partes Review (IPR) process. This process is more efficient, cost effective, and serves as an important check in the system to reverse mistakes, improve patent quality, and save money by allowing earlier generic drug competition. The IPR process could be improved by expanding the grounds for a challenge to a patent to include the lack of written description of a patent.

- Create a pre-grant opposition system similar to the one used by the USPTO for trademarks. Such a system could permit third parties to file legal challenges based on all available grounds used during examination to determine whether a patent application is valid. Pre-grant opposition systems permit knowledgeable experts to weigh in on the merits of a new patent application while it is still under review.

Unmerited patents listed in the Orange Book

Drugmakers typically file a series of strategic sequential patents in addition to the main patents covering the active ingredient in order to delay generic entry. These secondary and tertiary patents – which can cover formulations, polymorphs, new indications, and medical devices combined with off patent active ingredients – are often found unmerited or result in settlement agreements when litigated.

Some potential policy options to improve the administration of the FDA's Orange Book, speed up generic entry, and reduce litigation are:

- Update existing legislation to allow the removal of a patent from the Orange Book if it is invalidated using the Post Grant Review (PGR) or IPR processes. Currently, the language of the law requires the decision of a federal or appellate court to remove an invalidated patent.
- Improve the quality and transparency of the Orange Book. The FDA should be given greater authority for assessing which patents can be listed on the Orange Book to ensure that only necessary patents are included and it is not used by manufacturers to strategically delay competition through litigation. For example, the FDA could require brand name drug manufacturers to provide a patent attorney opinion letter explaining why a patent should be listed in the Orange Book and the letter could be publicly displayed on the Orange Book.



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