America's Overspend: How the Pharmaceutical Patent Problem is Fueling High Drug Prices

The American health system is poised to incur $55 billion in excess costs from pharmaceutical companies' strategies to delay competition on three drugs

EXECUTIVE SUMMARY

This analysis of three high-cost drugs for cancer and hepatitis C reveals that anti-competitive strategies by branded pharmaceutical companies are driving excess costs to American payers and patients. Product lifecycle management, whereby branded companies obtain unmerited patents to delay competition, is the primary strategy identified and evaluated by this study. A related strategy is "pay-for-delay": branded companies pay generics to stay off the market, a symptom of underlying unmerited patents and misaligned incentives in the patent and regulatory systems. The following three multi-billion dollar blockbuster drugs were all found to have questionable – and likely unmerited – patents that are providing excess exclusivity periods.

These unmerited patents and related anti-competitive strategies permit patent holders to delay competition from generic equivalents by decades, which in turn keeps prices artificially high for healthcare payers and taxpayers:

- **Revlimid® (lenalidomide):** Unmerited patents enable a minimum exclusivity period from 2019 through 2028. Payers are projected to spend $45 billion in excess costs for the drug within this period, prior to the first generic product entering the market.

- **Sovaldi® (sofosbuvir):** Unmerited patents will prevent competition from now through 2034, when final patents held by Gilead Sciences expire on the drug. Payers are projected to incur $10 billion in excess costs.

- **Gleevec® (imatinib):** In the one-year period from 2015-16, approximately $700 million dollars in excess costs were passed onto payers as a result of a pay-for-delay deal cut by Novartis to a generic company in exchange for delaying the entry of generic imatinib.

This analysis found that the American health care system is poised to incur $55 billion in excess costs in the next 15 years on these three drugs alone due to unmerited patents blocking generic competition.

INTRODUCTION

One in five American households reported not being able to fill a prescription in the last year due to the high costs of medicines.[1] States are being forced to ration or deny lifesaving medicines to patients, with newer specialty medicines causing budgets to crumble under the weight of skyrocketing prices.[2] The problem is getting worse: since 2008, the cost index for branded drug prices has nearly tripled,[3] and by 2025 prescription drug spending nationally is poised to double.[4] This trend is putting American patients and the sustainability of public payers at risk.

With 70% of American voters across the political spectrum identifying prescription drug pricing as a critical problem,[5] the need for solutions has gained national prominence. Despite the range of solutions being discussed at the state and national level, meaningful price reductions will not be possible without accelerated and increased competition. A vibrant generic drug market with two or more suppliers is the only type of healthy market that consistently and substantially lowers prescription drug prices by more than half.[6] **The lack of effective competition in the prescription drug market is due to monopolies that branded companies hold for decades with over-patenting and pay-for-delay strategies.**

The market for pharmaceuticals in the U.S. is inefficient and incentives in the drug development system are not aligned with desired outcomes. The continual extensions of market exclusivities enabled by a combination of out-of-date legislation and the range of tactics used by branded companies to delay competition have created an unbalanced marketplace. This paper examines the underlying patent portfolios and market behavior of three of the most expensive and widely used drugs in America in order to understand whether and how unmerited patents and related strategies are delaying generic competition and driving **overspend** on lifesaving medicines.

Overspend
The difference between the cost of a branded drug and its generic equivalent over the time period in which an unmerited patent was identified as preventing entry of a generic product.

METHODOLOGY

Drug Prioritization

To arrive at the highest-cost and most widely used small molecule prescription medicines in the U.S., this analysis compiled a list of all drugs that ranked on four different lists:

1) The top 20 drugs in overall spending in the U.S. in 2015[7]
2) The top 20 drugs in Medicare Part D spending in 2015[8]
3) The top 20 drugs in Medicaid spending in 2015[8]
4) The 64 unique drugs that met the criteria of being both reimbursed at $600 or more for a one-month prescription and had total annual gross reimbursement of more than $72 million dollars in 2015[9]

Twenty drugs appeared on three or four of these lists, or were on the list of 64 noted above and at least one other list. All biologics and injectables (insulin, monoclonal antibodies,

etc.) were excluded, resulting in a shortlist of twelve small molecule products. Given the in-depth nature of the patent review process (described below), this preliminary analysis focuses on three drugs. These drugs were selected as those that are the most widely reported to be causing significant financial strain to patients and purchasers[10-12] and ensuring that the analysis included different patent holder companies.

Shortlist of top 12 high cost small molecule drugs

Drug	Disease	Patent Holder
Abilify®	Bipolar disorder	BMS
Atripla®	HIV	Gilead
Gleevec®	**Oncology**	**Novartis**
Harvoni®	Hepatitis C	Gilead
Invega®	Antipsychotic	Johnson & Johnson
Latuda®	Schizophrenia	Sunovion Pharma
Lyrica®	Neuropathic pain	Pfizer
Revlimid®	**Blood related disorders**	**Celgene**
Sovaldi®	**Hepatitis C**	**Gilead**
Stribild®	HIV	Gilead
Tecfidera®	Multiple sclerosis	Biogen
Truvada®	HIV	Gilead

Patent Analysis[i]

Both patent landscaping and validity analyses were conducted on the three drugs in order to a) map all the key patents on each drug, b) identify the patent expiration dates and related FDA marketing exclusivity periods, and c) evaluate the validity of each patent.

Each patent and the scope of its protection was reviewed, including if the patent would be a barrier to competitors in order to operate freely and verifying if patents are listed on the U.S. FDA Orange Book. These are deemed the most important patents that a branded company would assert if a generic entrant were to file an Abbreviated New Drug Application (ANDA)[ii] to enter the market with a generic version. While the listed patents on the Orange Book are typically considered the higher value patents, other non-listed patents can also pose problems for potential generic entrants, and therefore all potential patent blocks to generic competition were assessed.

Finally, "prior art" or evidence searches and technical expert reviews were conducted to assess the validity of the patent for novelty and obviousness, the key measures of whether a patent is merited or not. Experience shows that the legal obviousness inquiry is often diluted in patent examination and court review of drug patents. For this reason, this scientific and legal evaluation focuses on a thorough application of the legal standard of obviousness.

Patent searches were conducted up until September 15th 2017.[iii]

Cost Modeling

For each drug, a cost model was built to quantify the financial impact of unmerited patents or pay-for-delay settlements blocking entry of generic products into the market over time. The models used a variety of real-world annualized market-based assumptions to assess the financial impact –excess costs incurred – that resulted from comparing *status-quo* market conditions (current expiry of patents on a drug) to those that reflected earlier entry of generic

[i] Detailed methods and results available upon request

[ii] The standard regulatory documentation and pathway by which generic products demonstrate equivalency to a branded product are reviewed and approved by the FDA

[iii] As patent applications in the United States are usually published after eighteen months, patent applications filed less than eighteen months before the search date were not captured. Also patent applications that were withdrawn before publication cannot be picked up in any search.

products. The model accounts for ANDA filing eligibility and assumes that the accelerated entry of a generic product to the marketplace is consistent with standard timelines for ANDA review and approval.

Other key variables considered annually in the analysis included:

- The total size of the patient pool and the number of patients coming onto treatment each year.
- The market share of the product being evaluated relative to the competitor landscape.
- Pricing and payer discounts and market dynamics for both branded and generic drug equivalents.
- The share of patients that can potentially benefit from generic products.

All models were created with clinical assumptions intended to reflect how the generic version of each drug would be used in the real-world setting. This included considerations for pairing generic equivalents with other drugs that may not have otherwise been possible given unmerited patents restricting such opportunities.

CASE STUDY ANALYSIS

Revlimid®

Developed by U.S. biopharmaceutical company Celgene, Revlimid® was first approved in the U.S. in 2006 to treat multiple myeloma. It has since been approved for multiple other hematology cancers and indications. It has been the main driver of Celgene's revenue growth in the past decade, netting the company $43 billion dollars to date, and comprising two thirds of the company's total annual revenue. Priced at over $125,000 per year of treatment, it ranks among the most expensive medicines available on the market. Moreover, Celgene has raised the price of the drug by more than 50% since 2012: today, a single 10mg tablet costs about $600. It is not just the list price of the drug that is high.[13] A recent study revealed that the median out-of-pocket cost for a Medicare patient on Revlimid® was $11,500 per year, the highest among other high-cost specialty drugs.[14]

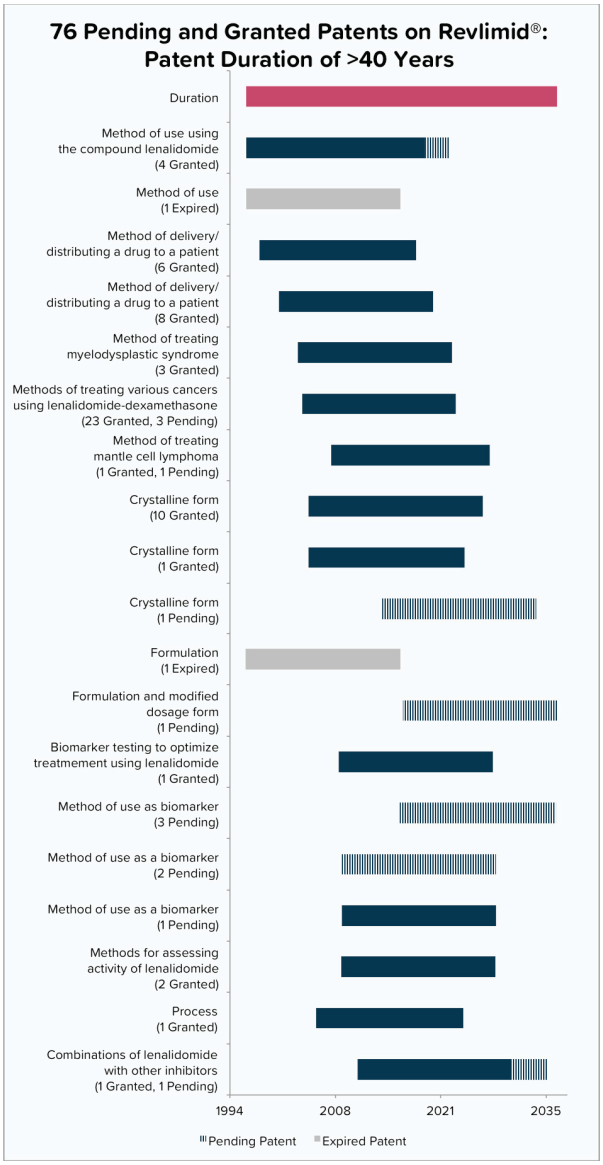
Patent Analysis

The compound used for Revlimid® is known as lenalidomide, a derivative of an older parent compound thalidomide, first marketed in 1957 as a sedative or hypnotic. Later, in the 1960s, it became public knowledge that this compound and its derivatives possessed anti-inflammatory properties. Research done by actors other than Celgene in the early 1990s showed that it could also be used to kill tumor cells.

The patent analysis identified a total of 76 granted patents and patent applications for Revlimid® (lenalidomide) as held by Celgene and related companies that have been acquired.[iv] In addition, there are 29 abandoned patent applications, making a total of 105. In total, including the pending patent applications, the combined patent protection for these drugs is potentially set to expire at the end of 2036, giving Celgene's Revlimid® patent portfolio a lifespan of at least 40 years.

[iv] For example, Signal Pharmaceuticals, Inc.

Revlimid® Patent Landscape



These 105 patents cover the various hematology cancers and indications for which Revlimid® has been approved. The landscape for Revlimid® comprises the following categories of patents which cover the various indications it has been approved for: methods of use and treatment, including biomarkers, crystalline forms, formulations, devices for assisting patients with filling their prescriptions and controlling distribution of lenalidomide, combination with other inhibitors, and processes for manufacturing lenalidomide. Typically, all these types of patents would be classified as secondary patents. Of the 66 currently granted patents on Revlimid®, 27 are listed on the U.S FDA Orange Book.

This expert review showed that in light of the prior art available in the field, there is a substantial body of evidence to suggest that all of these granted patents and pending patent applications protecting Revlimid® would be unmerited if the legal standards of novelty and obviousness were applied. Overall, this assessment concludes that Celgene developed a thicket of patents as a defensive strategy to protect Revlimid® in order to maximize its monopoly hold as long as possible and block generic competition. Indeed, generic versions should be able to enter the market at least in October 2019.[v]

This assessment is supported by the settlement between Celgene and Natco, who challenged the very first patent on Revlimid®. Indeed, numerous other generic companies are currently in litigation with Celegene over its various patents. This suggests Celegene's entire patent portfolio, from the first patent listed on the Orange Book to the latest pending ones for Revlimid®, is built on unmerited patents.

Cost Analysis

Excess costs associated with unmerited patents on Revlimid® were analyzed over a five-year period: from October 2019 when the main

[v] While out of the scope of this paper, though consistent with the over-patenting strategies used by Celgene to thwart generic competition, the company has also been accused of REMS abuses: intentional efforts by branded companies to restrict generic companies from gaining access to product samples in order to conduct bioequivalence studies. These so-called REMS abuses have been cited as a major tactic by branded companies to delay the introduction of generic products to the market.

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